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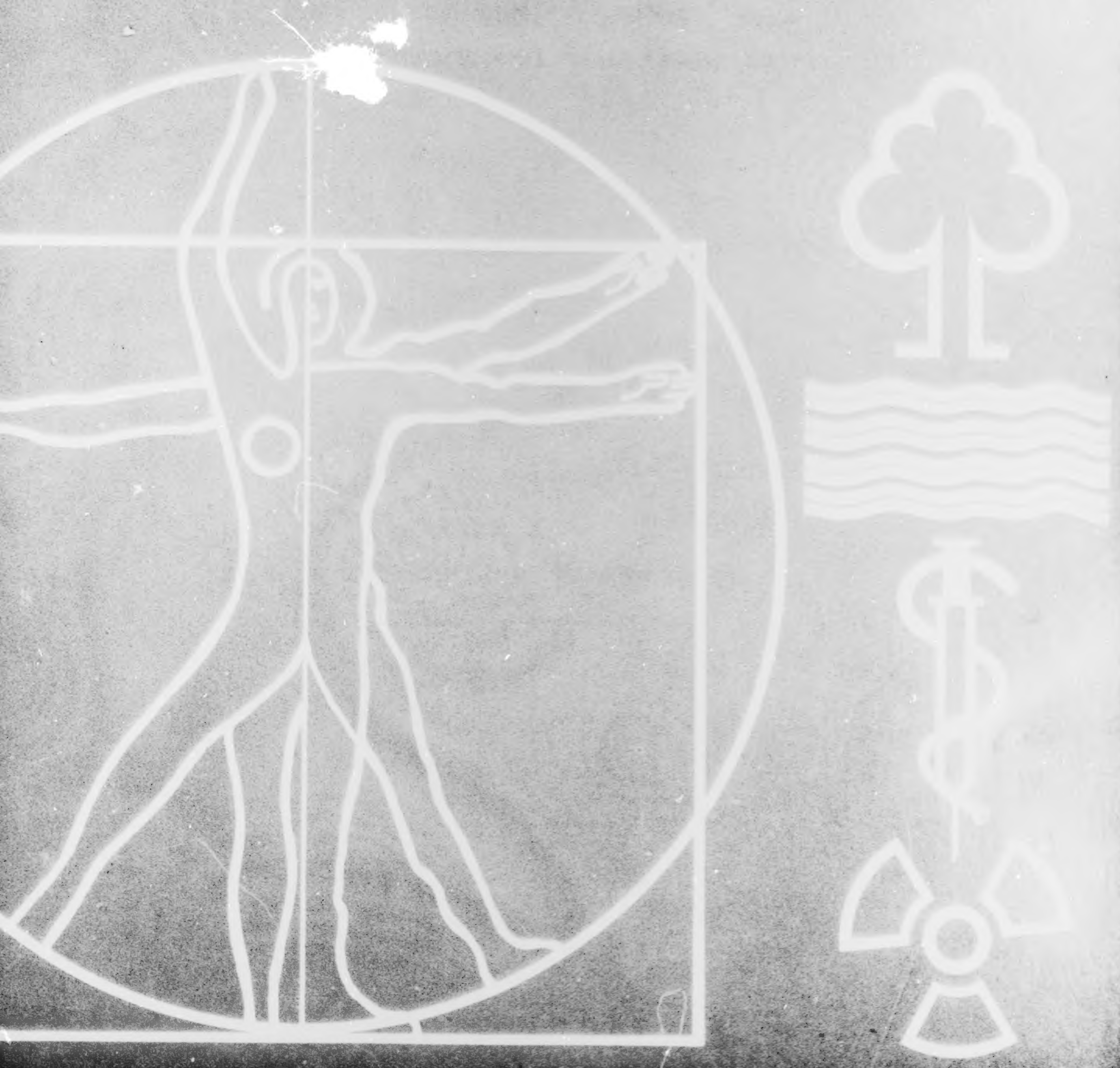
# chloronaphthalenes: an environmental-health perspective



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# CHLORONAPHTHALENES:
# AN ENVIRONMENTAL-HEALTH PERSPECTIVE

Environmental Health Directorate

Health Protection Branch

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# ABSTRACT

The report is a review of the available information pertinent to an environmental health assessment of chloronaphthalenes, and concerns: their chemical and physical properties, the methods used in their analysis, their commercial use with particular reference to the situation in Canada, their behaviour in the environment, and the potential health effects of the compounds. In addition, regulations governing chloronaphthalenes adopted by some countries are summarized.

It is concluded, from the review, that exposure of the Canadian population to chloronaphthalenes is probably extremely low and that the compounds are unlikely to present an environmental health problem in Canada. It is emphasized, however, that data are insufficient to assess definitively the environmental behaviour of the compounds. In addition, no data were found from which the health effects, if any, of continuous long-term exposure to very low concentrations of chloronaphthalenes can be predicted.

It is pointed out that research in a number of areas would be necessary before a definitive environmental health assessment of chloronaphthalenes could be made. Such research would include monitoring of environmental levels, measurement of basic physical and chemical properties of the compounds, and a toxicological assessment of chloronaphthalenes.

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# SUMMARY

Chloronaphthalenes, first used commercially at the beginning of this century, have been known to cause occupationally related disease and occasionally death among workers exposed to their fumes. Because of this, occupational exposure limits were set by a number of countries.

Chloronaphthalenes have been used in a diversity of commercial products in the past; particularly as dielectrics, and as impregnants and coatings in paper and textile products. The compounds, however, are nowadays used commercially to only the most minimal extent, and, in Canada, not at all. Similar to polychlorinated biphenyls, to which chloronaphthalenes bear some chemical similarity, they may be environmentally persistent and may concentrate in the food chain. (Indeed, chloronaphthalenes have been detected in environmental samples and in human tissue.) There was a fear that chloronaphthalenes might present an environmental health problem and at least two countries, the United States and Japan, enacted legislation aimed at preventing environmental release of the compounds.

## BASIC INFORMATION CONCERNING CHLORONAPHTHALENES

There are 75 chlorinated naphthalenes, of which some 55 have been individually synthesized and characterized. Commercial products were mixtures of chloronaphthalenes, usually of incompletely defined and variable composition.

### Synthesis and Manufacture

Except for 1-chloronaphthalene and octachloronaphthalene, which can be prepared by direct chlorination of naphthalene, individual chloronaphthalenes must be prepared by indirect routes. Synthesis of the compounds involves, by and large, the displacement by chlorine of certain substituent groups in chosen substituted naphthalenes. Chloronaphthalenesulphonyl chlorides, chloronaphthalenesulphonic acids, naphthoyl chlorides, and naphthols (as substituted naphthalenes) and phosphorus pentachloride, hydrochloric acid and copper(II) chloride (as chlorinating agents) have all been used.

Commercial chloronaphthalenes, on the other hand, were commonly manufactured by reacting chlorine gas with molten naphthalene in the presence of iron(III) or antimony(V) chloride. Addition of chlorine was stopped when the product mixture had reached the desired degree of chlorination.

## Properties

Chloronaphthalenes are water insoluble, waxy solids possessing a high degree of chemical and thermal stability. Their physical properties change as chlorine content increases; boiling and melting points generally increasing, vapour pressure and water solubility generally decreasing.

Melting points range from about -3°C for 1-chloronaphthalene to above 200°C for some tetrachloronaphthalenes. Boiling points are high and for the more highly chlorinated naphthalenes are probably above the decomposition temperature of the compounds. The commercial products, being mixtures of chloronaphthalenes, have ill-defined melting points and boiling points.

Chloronaphthalenes have good solubility in chlorinated and aromatic solvents and in petroleum naphthas, but have limited solubility in ethers and mineral oils. For most practical purposes, chloronaphthalenes are insoluble in alcohols and water -- the majority likely having water solubilities in the ppb range. Chloronaphthalenes also possess very low volatility, with room-temperature vapour pressures calculated to be tenths of a pascal and lower.

Chloronaphthalenes, in common with aromatic hydrocarbons in general, display three absorption bands in the ultraviolet spectral region above 200 nm as a result of $\pi-\pi^*$ electronic transitions. The maximum absorption occurs in the region 220 to 250 nm but slight, although still significant, absorption occurs in the 300 nm region. Chloronaphthalenes also exhibit complex infrared spectra in the region 1650 to 660 $cm^{-1}$, with a number of strong bands arising from out-of-plane deformation vibrations of hydrogen atoms attached to the naphthalene nucleus.

## Analysis

Chloronaphthalenes are analyzed by methods similar to those used for polychlorinated biphenyls and organochlorine pesticides. The most extensively used analytical technique is gas liquid chromatography, although high performance liquid chromatography and thin layer chromatography have also been widely employed. Mass spectrometry and voltammetry have been less extensively used.

Chloronaphthalenes can be extracted from environmental samples (water, soil, tissue) using a variety of organic solvents -- toluene, hexane and diethyl ether being the most common. Chloronaphthalenes in the atmosphere must first be trapped by drawing air through a suitable filter. Polyurethane foam is the most widely used material, although Amberlite® XAD-2 resin and activated carbon have also been employed. The trapped compounds are then extracted with organic solvents.

The large number of organochlorine compounds that may be present in environmental samples (notably polychlorinated biphenyls and organochlorine pesticides) necessitate clean-up procedures and differentiation techniques to isolate the chloronaphthalenes. Column chromatography is frequently employed to separate chloronaphthalenes (along with polychlorinated biphenyls) from organochlorine pesticides. Silica gel or alumina are the most usual stationary phase and hexane is normally the eluant. To simplify analysis of the resultant mixture of chloronaphthalenes and polychlorinated biphenyls, conversion of the compounds to a single derivative for each class is sometimes used. One option is to exhaustively chlorinate the mixture to yield solely octachloronaphthalene and decachlorobiphenyl. An alternative is dehydrochlorination of the mixture to yield the parent hydrocarbons, naphthalene and biphenyl. Either option allows easy identification and quantification of chloronaphthalenes in the presence of polychlorinated biphenyls. These differentiation techniques, however, only provide measurement of total chloronaphthalenes in the sample, and the individual chloronaphthalenes are not identified.

## CHLORONAPHTHALENES IN THE ENVIRONMENT

Little systematic work has been carried out on the release, subsequent transport and eventual fate of chloronaphthalenes in the environment, and only fragmentary information exists. Chloronaphthalenes have been detected in environmental samples -- in biota, in soils and aquatic sediments, and in the atmosphere surrounding chloronaphthalene manufacturers -- in many parts of the world. In most cases, chloronaphthalenes were found associated with, but in significantly lower concentrations than, polychlorinated biphenyls.

### Environmental Sources

Because chloronaphthalenes are no longer used in Canada, any compounds found in the Canadian environment at the present time would have arisen from past use of the compounds or from products and processes not directly connected with such use.

The largest use of chloronaphthalenes in the 1970s was as a dielectric in small capacitors, particularly those for automotive ignition systems. Such capacitors are commonly changed whenever an automative engine is tuned and solid waste disposal sites may well have become a minor reservoir of chloronaphthalenes. Effluents from textile dyeing facilities (which may have used chloronaphthalene-based dyes) and electroplating processes (which may have used chloronaphthalene-containing electroplating stop-off compounds) may have contained chloronaphthalenes. Thus the compounds may well have been introduced into sewage sludge. It has been speculated also that chlorination of naphthalene (a known water pollutant) during water treatment activities may be a continuing environmental source of chloronaphthalenes. In addition, chloronaphthalenes have been identified as minor contaminants in commercial polychlorinated biphenyls and consequently, because of the widespread environmental distribution of polychlorinated biphenyls and their continued if restricted use, these compounds may also be considered a current environmental source of chloronaphthalenes.

## Environmental Transport and Fate

Chloronaphthalenes in the environment will be transported within the atmospheric and aquatic systems, with exchange between the two. The low volatility of chloronaphthalenes suggests that, in a global sense, atmospheric dispersion would be strictly a local phenomenon. Similarly, because of the low water solubility of the compounds, transport of chloronaphthalenes in solution by water would be slight. It has, however, been speculated that chloronaphthalenes may be readily adsorbed by organic-containing particulates in natural water and that such adsorption could be an important transport process. Because data are lacking, little can be said concerning transfer functions of chloronaphthalenes between water and the atmosphere, except analogy with other water insoluble pollutants of low volatility suggests that such exchange may occur.

## Environmental Degradation

Because of their physical and chemical stability, chloronaphthalenes would not be expected to be readily degraded in the environment. However, the results from laboratory studies of photochemical reactions of chloronaphthalenes suggest that photolysis may be a minor degradation pathway.

Although the biodegradation of monochloronaphthalenes has been demonstrated under certain conditions, it is probably safe to speculate that chloronaphthalenes, like other organochlorine pollutants, will generally be resistant to environmental biodegradation.

## Environmental Sinks

Octanol/water partition coefficients for chloronaphthalenes have been predicted, on the basis of theoretical calculations, to lie within the range $10^4$ for monochloronaphthalenes to $10^9$ for octachloronaphthalene. Such values indicate a moderate ability of the compounds to concentrate in soils and sediments, and in biota. Although a few reported measurements of chloronaphthalenes in the environment do indeed show an apparent tendency for the compounds to concentrate in sediments and biota, no studies which have unambiguously identified and quantified such concentration effects have been carried out.

## HUMAN HEALTH EFFECTS

The concern over chloronaphthalene poisoning in humans resulted from the occurrence of skin disease (chloracne) and systemic effects in workers, attributable to contact with, and/or inhalation of, chloronaphthalenes in the course of various manufacturing processes. A chloracne or "cable rash" was a common result of prolonged skin contact with chlorinated naphthalenes, linked to some degree with poor hygienic habits. The skin disease was marked by the formation of comedones in the acini of pilosebaceous glands of the skin, progressing to inflammatory reactions and gland destruction.

Systemic responses have been shown to involve a wide range of tissues and organs and could be seriously debilitating with progressive renal and hepatic damage. Fatalities were correlated with inhalation of chloronaphthalene fumes, associated with extensive tissue and organ lesions, particularly a yellow liver atrophy marked clinically by icterus. Many case histories report extensive liver damage and death to be a latent response, occurring weeks to months after removal from the source of chloronaphthalene poisoning. This may be attributed to a continued release into circulation of chloronaphthalenes from storage in fatty tissues. Recovery from chloronaphthalene poisoning, whether the manifestations were chloracne or systemic effects, generally ranged from several months to more than a year.

There has been no quantification of occupational exposure levels resulting in toxicity responses in humans. Toxicity studies in laboratory animals, and comparative assessments of exposures in domestic animal species, have tried to model toxicity responses in humans and to establish dose-response relationships. The laboratory rat was found to be relatively refractory to chloronaphthalene exposure, surviving dietary exposures of 15 mg/day per rat and inhalation levels of 10 mg/m$^3$ for several months without untoward signs of intoxication. Cattle show another extreme, being highly sensitive and exhibiting bovine hyperkeratosis (X-disease) at very low-level exposures, and death after a single exposure of 1.0 g in the calf. Altogether, the various species differ greatly both in sensitivity to chloronaphthalenes and in the expression of toxicity. The rabbit was determined to be the most suitable for demonstrating chloracne. No single species, however, was found to exhibit all of the responses recorded in humans.

Chloronaphthalenes can be absorbed through the skin, lungs and gut, and tend to deposit in fatty reservoirs. Accumulation occurs in pilosebaceous acini and adipose tissue, and to a lesser degree in brain, kidney and other body tissues. Excretion occurs through urine and bile, and predominantly by the urinary excretion of conjugated metabolites. Hepatic microsomal oxygenases have been shown to be inducible by chlorinated naphthalenes, but the relationship of these reactions to chloronaphthalene detoxification, or perhaps a potentiation of chloronaphthalene toxicity, has not yet been defined.

Although the animal data are disparate it is possible to say that, in combination with findings from occupational exposures, the mono- and dichloronaphthalenes are relatively non-toxic or of low toxicity. This also tends to be the case for octachloronaphthalene. It is the tetra-, penta- and hexachloronaphthalenes which contribute most to chloronaphthalene toxicity. A dose-response relationship is implicated, although it is not possible to quantify this for human exposures. In humans, the toxicity effects of chloronaphthalenes tend to be progressive, becoming generalized to encompass many organs and systems at high doses. No sex or age dependency in the manifestation of toxicity has been confirmed in the occupationally exposed population.

## CONCLUSIONS

It is virtually certain that exposure of the Canadian population to chloronaphthalenes is extremely low -- the compounds appear not to have been used for some years, their environmental transport is limited, and environmental degradation (albeit at a slow rate) may occur by photolytic and biological action. These factors and the toxicity data from the available clinical literature suggest that chloronaphthalenes are not likely to present an environmental health problem in Canada.

A limited caveat, though, is in order. Environmental monitoring results indicate chloronaphthalenes in some biota, suggesting that the compounds may have entered the human food chain. Calculated octanol/water partition coefficients suggest that the compounds may bioaccumulate. And there are no studies from which the health effects, if any, of continuous long-term exposure to very low concentrations of chloronaphthalenes can be predicted.

## RECOMMENDATIONS

The data on which to make a definitive environmental health assessment of chloronaphthalenes are far from complete. To make such an assessment, research into the following areas would be necessary:

1. Comprehensive monitoring of chloronaphthalenes in the Canadian environment should be carried out, with particular emphasis on the measurement of levels in drinking water and food. Analytical techniques necessary to accomplish this task are well developed.

2. If significant environmental levels are encountered, more information concerning the basic properties of chloronaphthalenes will have to be obtained. Measurement of water solubilities, vapour pressures and octanol/water partition coefficients under a variety of physical conditions would provide information useful in predicting how the compounds are transported in the environment and whether they would tend to concentrate in the food chain. Determination of the rates of hydrolysis, photolysis and biological degradation under realistic environmental conditions would provide information on the potential environmental persistence and mass balance of the compounds.

3. Toxicological assessment of chronic exposure to low levels of chloronaphthalenes is needed. Such studies are difficult, however, because no animal species is indicated clearly as a comprehensive model of the human condition.

Because chloronaphthalenes are apparently no longer commercially used in Canada such a research effort, while important to increasing knowledge of the potential environmental health effects of the compounds, may be considered to be impractical.

# 1. INTRODUCTION

The first chloronaphthalenes, in their crude form, had the consistency of congealed olive oil (l'huile d'olive figée) -- a culinary description provided by their discoverer, Auguste Laurent, in 1833 [1]. He was able to separate two compounds formed by the reaction of chlorine gas with naphthalene, one a light yellow oily substance and the other a white granular solid. These compounds were probably impure samples of the two monochloronaphthalenes, 1-chloronaphthalene and 2-chloronaphthalene, the first of 75 compounds that comprise the group variously referred to as chlorinated naphthalenes, polychloronaphthalenes, polychlorinated naphthalenes or, simply, chloronaphthalenes. In this report we have used "chloronaphthalenes" to refer to the group as a whole, except where to do so would create ambiguity.

The thermal and chemical stability, and water insolubility of the compounds led to their use in a diversity of commercial products, particularly as dielectrics and as impregnants and coatings in paper and textile products. However, chloronaphthalenes are not now used commercially to more than the most minimal extent. But the compounds have been detected in the environment and in human tissue, and, by analogy with polychlorinated biphenyls with which chloronaphthalenes bear some chemical similarity, they may be environmentally persistent and concentrate in the food chain. These factors and the demonstrated toxicity of some chloronaphthalenes have led to concern that they may present an environmental health problem.

Because information is incomplete in many areas, a rigorous environmental health assessment of chloronaphthalenes cannot be made. Instead, this report reviews the available information with emphasis, where possible, on the Canadian situation. The purpose of the report is to provide a corpus of information concerning the compounds for the Environmental Health Directorate of Health and Welfare Canada. It is hoped that this collection of data will facilitate decisions on whether or not further investigations are warranted to elucidate more thoroughly the possible effects of chloronaphthalenes on the health of Canadians.

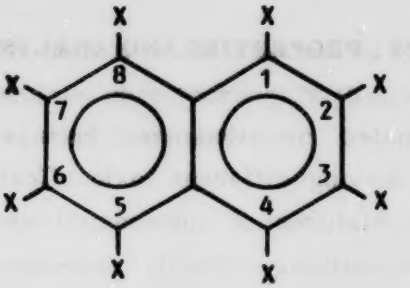
# 2. IDENTITY, PROPERTIES AND ANALYSIS

There are 75 chlorinated naphthalenes, each exhibiting different properties and potentially having different toxic effects. The commercial products, however, were mixtures of chloronaphthalenes, usually of ill-defined and variable composition. Ideally, assessment of the health implications of these commercial products would be based on identification of all their component chloronaphthalenes and on the properties (physical, chemical, toxicological) of each constituent. Such information is, at best, incomplete, and usually lacking. This chapter reviews published material dealing with structure and identity of the compounds, their physical and chemical characteristics, and the methods used in their analysis.

## 2.1 STRUCTURE AND IDENTITY

### 2.1.1 Structure

Chloronaphthalenes are compounds where any or all of the eight hydrogen atoms in naphthalene are substituted by chlorine atoms (Figure 2-1). The molecules have an essentially planar configuration, with the possibility that some of the chlorine atoms would be forced slightly out of the plane of the naphthalene nucleus by steric hinderance from adjacent hydrogen (or chlorine) atoms [2]. The $\pi$-electrons are to a large extent delocalized, thereby conferring an aromatic character to the molecules; this delocalization is represented in structural formulae by a circle within each fused benzene ring. The degree of $\pi$-electron delocalization in the naphthalene nucleus is not as extensive as it is in benzene, and some of the carbon-carbon bonds may be considered as exhibiting a slight olefinic character [4]. This slight deviancy from carbon-carbon bond equivalency is shown by the fact that the different carbon-carbon bonds within the naphthalene nucleus are not all of the same length (see Figure 2-1). The carbon-carbon bond lengths in chloronaphthalenes are virtually the same as those in naphthalene [2].



$C_{10}H_{(8-y)}Cl_y$

X = H or Cl

Approximate bond lengths [2]:
(based on 1,3-dichloronaphthalene)

1-2, 3-4, 5-6, 7-8 = 0.136 nm
1-9, 4-10, 5-10, 8-9 = 0.142 nm
2-3, 7-6 = 0.142 nm
9-10 = 0.141 nm
C-Cl = 0.176 nm

FIGURE 2-1 Structure of Chloronaphthalenes

TABLE 2-1 Number of Chloro Derivatives of Napthalene*

| Degree of Cl substitution | No. of Cl atoms in one ring | No. of Cl atoms in other ring | No. of possible chloronaphthalenes |
|---|---|---|---|
| mono- | 0 | 1 | 2 |
| di- | 0 | 2 | 4 |
| | 1 | 1 | 6 |
| tri- | 0 | 3 | 2 |
| | 1 | 2 | 12 |
| tetra- | 0 | 4 | 1 |
| | 1 | 3 | 8 |
| | 2 | 2 | 13 |
| penta- | 1 | 4 | 2 |
| | 2 | 3 | 12 |
| hexa- | 2 | 4 | 4 |
| | 3 | 3 | 6 |
| hepta- | 3 | 4 | 2 |
| octa- | 4 | 4 | 1 |
| TOTAL | | | 75 |

* Derived from Brinkman and Reymer [3]

### 2.1.2 Number of Chloronaphthalenes

Brinkman and Reymer state in their extensive review of chloronaphthalenes [3]: "Theoretically 75 different PCNs (chloronaphthalenes) exist ... However, on mechanistic and statistical grounds it is unlikely that all of them are formed in technical chlorination processes. More important, physically, the difficulty of isolating isomers from the mixtures produced by chlorination of naphthalene is such that indirect routes must be employed for all individual PCNs except 1-monochloro- and octachloronaphthalene. So far, synthesis of 55 individual PCNs has been reported."

Table 2-1, derived from information presented by Brinkman and Reymer [3], shows the number of possible chloronaphthalene isomers for different degrees of chlorination of the naphthalene nucleus. There are two isomers possible for each of the monochloro- and heptachloro-substituted naphthalenes; 10 isomers of each of the dichloro- and hexachloro-substituted naphthalenes; 14 isomers of each of the trichloro- and pentachloro-substituted naphthalenes; 22 isomers of tetrachloronaphthalenes; and, of course, only one octachloronaphthalene.

The variety of chlorinated naphthalenes presents a considerable analytical problem if complete characterization of chloronaphthalenes found in environmental samples is desired. A toxicological assessment of chloronaphthalenes presents a greater problem. There is no detailed evaluation of structure/toxicity relationships beyond an apparently observed change in toxicity with degree of chlorination (see Chapter 5).

### 2.1.3 Composition of Commercial Chloronaphthalenes

Commercial chloronaphthalenes were produced and sold in the United States as refined chloronaphthalenes and as chloronaphthalene crudes. The crudes (a minor fraction of the products sold), with essentially the same physical properties as the refined products, although not held within as close limits, were suitable for many applications where dark colours were acceptable. The commercial products may have contained impurities resulting from chlorination of impurities originally present in the coal-tar or petroleum derived naphthalene. Impurities which may have been present in commercial naphthalene include biphenyls, fluorenes, pyrenes, anthracenes and dibenzofurans [5].

The results of gas chromatographic analyses of some Halowaxes* are shown in Table 2-2. These commercial products were obviously quite complex mixtures, especially when it is remembered that a number of isomers would be possible for each level of chlorination. There is broad agreement between these analyses and the compositions (Table 3-2) reported by the manufacturer.

## 2.2 PREPARATION AND MANUFACTURE

While the manufacture of chloronaphthalenes is largely of historical interest, the synthesis of individual chloronaphthalenes is important to analysts because standard compounds are required to identify chloronaphthalenes detected in environmental samples.

### 2.2.1 Preparation of Chloronaphthalenes

Except for 1-chloronaphthalene and octachloronaphthalene, which can be prepared by direct chlorination of naphthalene, individual chloronaphthalenes must be prepared by indirect routes. These syntheses may be accomplished in a number of ways and involve the displacement by chlorine of certain substituent groups in chosen substituted naphthalenes. Rodd's Chemistry of Carbon Compounds [7] details the following: the hydroxyl group in naphthols can be replaced by chlorine if they are reacted with phosphorus pentachloride; dinitronaphthalenes may be irradiated in acetic acid containing hydrogen chloride to give the corresponding dichloronaphthalenes; naphthoyl chlorides can be converted, in excellent yields, to the

## TABLE 2-2 Experimentally Measured Composition of Some Halowaxes®

| | Halowax® | | | | | |
|---|---|---|---|---|---|---|
| Constituent | 1000 | 1001 | 1013 | 1014 | 1051 | 1099 |
| naphthalene | 4.4% | | | | | |
| mono- | 72.1 | | | | | |
| di- | 19.1 | 6.1% | | | | 6.7% |
| tri- | 0.3 | 54.4 | | 3.3% | 6.0% | 45.3 |
| tetra- | 1.2 | 30.89 | 46.0% | 16.0 | 12.8 | 27.4 |
| penta- | 1.8 | 5.1 | 47.8 | 33.0 | 11.2 | 16.1 |
| hexa- | | | 1.0 | 13.8 | | |
| octa- | | | | | 50.3 | |
| unidentifed naphthalenes | 1.0 | 3.3 | 11.2 | 24.0 | 16.6 | 4.4 |
| unidentified non-naphthalene constituents | | | | 9.0 | 4.6 | |
| TOTAL* | 99.9 | 100.0 | 106.0 | 99.1 | 101.5 | 99.9 |

These approximate percentage compositions were obtained from the peak areas of gas chromatograms presented by McKinney et al. [6]. The number of chlorine atoms were identified by the authors from mass spectrograms of the chromatographic eluate.

* That the peak areas do not add to 100 per cent in every case is probably a reflection of varying detector response for the different chloronaphthalenes and, perhaps, incomplete peak resolution in some of the chromatograms.

corresponding chloronaphthalenes by the use of chloro-tris(triphenylphosphine)-rhodium; and naphthalenesulphonic acids and their salts yield the corresponding chloronaphthalenes when fused with copper (II) chloride.

The most useful summary of synthetic methods is that of Brinkman and Reymer [3] in their review of chlorinated naphthalenes. It is from this review that the following descriptions of synthetic methods are taken.

Much of the synthetic work on chloronaphthalenes has been the result of investigations by Wynne and co-workers over a nearly 60-year period [8]. Their syntheses involved heating, at about 200°C, a chloronaphthalenesulphonyl chloride (or sulphonic acid) with phosphorus pentachloride for several hours. The required sulphonyl chloride may be obtained by heating a suitable lower chloro-substituted naphthalene with chlorosulphonic acid. If a sulphonic acid was required instead of a sulphonyl chloride, it could be obtained by treating chloro-substituted naphthalene with oleum. Hydrolysis of a naphthalenesulphonyl chloride with hydrochloric acid is an alternative route, in which event no additional chlorine atom is introduced into the naphthalene nucleus. The reaction schemes shown in Figure 2-2 give a general idea of these synthetic pathways.

Alternative routes summarized by Brinkman and Reymer [3] include: treatment of chlorotetralins with boiling sodium ethoxide; treatment of polynitro- or chloronitronaphthalenes with phosphorus pentachloride or concentrated hydrochloric acid; treatment of chloronaphthoquinone with phosphorus pentachloride; and decarboxylation of a polychloronaphthalene tetracarboxylic acid with copper carbonate in quinoline.

Octachloronaphthalene is prepared by exhaustive chlorination of naphthalene with chlorine and phosphorus pentachloride or with chlorine in

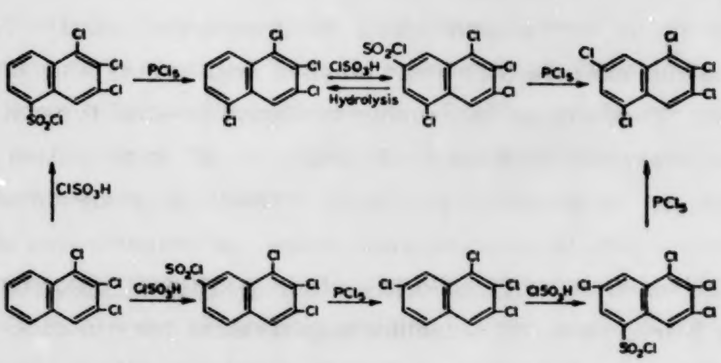


**FIGURE 2-2** **Some Reaction Schemes for the Synthesis of Chloronaphthalenes***

*** Developed by Brinkman and Reymer [3] as a simplification of an illustration of reaction schemes originally presented by Turner and Wynne [8].**

the presence of iron and iodine at 100 to 150°C. Treatment of octachloronaphthalene with lithium aluminum hydride yields 1H-hepta-chloronaphthalene.

### 2.2.2 Manufacture of Chloronaphthalenes [3]

Commercial chloronaphthalenes were generally produced by chlorinating naphthalene with chlorine gas in the presence of about 0.5 wt.% of iron (III) or antimony (V) chloride. Chlorination was begun at 80°C and the temperature slowly increased as the reaction proceeded. When the desired pour point had been reached, the chlorinated product was neutralized by stirring it, in the molten state, with aqueous alkali. The crude chloronaphthalene mixture was then washed with water and finally dried under vacuum. There is an increasing tendency in this type of process towards the simultaneous formation of products of substitution and addition of chlorine as chlorination proceeds. Thus, if chlorination was continued beyond the octachloronaphthalene stage, at temperatures above 200°C in the presence of iron (III) chloride, four additional chlorine atoms would be readily introduced and octachloronaphthalene terachloride would be formed; at the same time, liberation of carbon tetrachloride leading to the formation of perchloroindane would have occurred.

## 2.3 PHYSICAL PROPERTIES

In general, chloronaphthalenes are water insoluble waxy solids exhibiting a high degree of chemical and thermal stability. Their physical properties vary with the degree of chlorination. Only 1-chloronaphthalene is liquid at room temperature. As the chlorine content increases, the specific gravity, boiling point, melting point and fire point all increase while vapour pressure and water solubility decrease [5].

### 2.3.1 Melting Points and Boiling Points

2.3.1.1 Pure compounds: Since Armstrong and Wynne commenced systematic study of chloronaphthalenes in the 1880s [9], scores (and perhaps hundreds) of papers containing information on the melting and boiling points of chloronaphthalenes have been published. In many of these publications it is unclear as to how pure the compounds were, and the task of compiling tables of melting points and boiling points is not an easy one. A number of such tabulations, of varying degrees of completeness, have been published in recent reviews of chlorinated naphthalenes [3,7,10,11]. The most comprehensive is the review by Brinkman and Reymer [3] and it was from this source that the data presented in Table 2-3 were obtained. The melting points range from about -3°C for 1-chloronaphthalene to values of above 200°C for some tetrachloronaphthalenes. Boiling points are high and for the majority of the more highly chlorinated naphthalenes are probably above the decomposition temperatures of the compounds.

2.3.1.2 Commercial compounds: Commercial chloronaphthalenes are mixtures and therefore have ill-defined melting points and boiling points. Some of these melting points and boiling points are summarized in Table 2-4. The melting points are not true melting points, but rather are the temperatures at which the material starts to soften. The commercial products boil over a range of temperatures which reflect the boiling points of the individual chloronaphthalenes in the mixture.

### 2.3.2 Solubility

Chloronaphthalenes have good solubility in chlorinated and aromatic solvents and in petroleum naphthas. They have limited solubility in ketones, ethers and mineral oils, and are, for all practical purposes, insoluble in alcohols and water [3]. There is, however, one experimentally measured value for the water solubility of a chloronaphthalene reported in the literature -- 4.66 μg/L for 1,2,3,4-tetrachloronaphthalene [13]. In

TABLE 2-3 Melting and Boiling Points of Individual Chloronaphthalenes [3]

| Chloronaphthalene | mpt. (°C)* | bpt. (°C) |
|---|---|---|
| 1- | -4 to -2.3 | 259.3 (@ 101.3 kPa) |
| 2- | 58 to 60 | 256 |
| 1,2- | 34 to 37 | 295 to 298 |
| 1,3- | 61.5 to 62 | 291 (@ 103.3 kPa) |
| 1,4- | 68 to 72 | 286 to 287 (@ 98.6 kPa) |
| 1,5- | 106.5 to 107 | sublimes |
| 1,6- | 48.5 to 49 | sublimes |
| 1,7- | 61.5 to 64 | 285 to 286 |
| 1,8- | 88 to 89.5 | decomposes |
| 2,3- | 119.5 to 120.5 | |
| 2,6- | 135 to 141 | 285 |
| 2,7- | 114 to 116 | |
| 1,2,3- | 81 to 84 | |
| 1,2,4- | 92 | |
| 1,2,5- | 74 to 79 | |
| 1,2,6- | 90 to 92.5 | |
| 1,2,7- | 88 | |
| 1,2,8- | 83 | |
| 1,3,5- | 102 to 103 | |
| 1,3,6- | 80.5 to 81 | |
| 1,3,7- | 112.5 to 113 | |
| 1,3,8- | 89.5 | |
| 1,4,5- | 130 to 131 | |
| 1,4,6- | 65 to 68 | |
| 1,6,7- | 109 to 109.5 | |
| 2,3,6- | 90 to 91 | |
| 1,2,3,4- | 196 to 198 | |
| 1,2,3,5- | 141 | |
| 1,2,3,7- | 115 | |
| 1,2,4,6- | 111 | |
| 1,2,4,7- | 140 to 144 | |
| 1,2,5,6- | 164 | |
| 1,2,5,7- | 114 | |
| 1,2,6,8- | 125 to 127 | |
| 1,3,5,7- | 178 to 181 | |
| 1,3,5,8- | 131 | |
| 1,3,6,7- | 119 to 120 | |
| 1,4,5,8- | 183 | |
| 1,4,6,7- | 139 | |
| 2,3,6,7- | 135 | |
| 1,2,8,x- | 135 | |
| 1,4,5,x- (x = 3?) | 144 | |
| 2,3,6,x- | 218 | |
| x,x,x,x- | 176 | |
| 1,2,3,4,5- | 168.5 | |
| 1,2,3,4,6- | 147 | |
| 1,2,3,5,7- | 171 | |
| 1,2,3,5,x- | 177 | |
| 1,2,4,6,x- (x = 8?) | 135 | |
| 1,3,5,8,x- | 155 | |
| 1,4,6,7,x- (x = 2?) | 131 | |
| 1,2,3,4,5,6- | not reported | |
| 1,2,4,5,6,8- | 175 to 177 | |
| 1,2,3,4,5,6,7- | compound impure | |
| 1,2,3,4,5,6,8- | 194 | |
| 1,2,3,4,5,6,7,8- | 197.5 to 203 | |

* The range of values found in the literature by Brinkman and Reymer [3]

**TABLE 2-4 Melting Points and Boiling Points of Some Commercial Chloronaphthalenes**

| Product | Physical Form | Approx. Cl Content (wt.%) | Approx. mpt. (°C) | Initial bpt. (°C @ 101.3 kPa) | Reference |
|---|---|---|---|---|---|
| Halowax 1031 | liquid | 22 | -25 | 250 | [12] |
| Halowax 1000 | liquid | 26 | -33 | 250 | |
| Halowax 1001 | flakes | 50 | 93 | 308 | |
| Halowax 1099 | flakes | 52 | 102 | 315 | |
| Halowax 1099B | flakes | 52 | 115 | 322 | |
| Halowax 1013 | flakes | 56 | 120 | 328 | |
| Halowax 1014 | flakes | 62 | 137 | 344 | |
| Halowax 1051 | powder | 70 | 185 | 310°C @ 4 kPa | |
| Nibren D88 | powder or flakes | 49 to 50 | 92 to 96 | | [10] |
| Nibren D116N | powder or flakes | | 113 | | [3] |
| Nibren D130 | powder or flakes | 59 | 130 | | [10] |
| Seekay R68 | wax | 46.5 | the mpts. of Seekay waxes were in the range 67-73°C to 120-125°C | | [3,10] |
| Seekay R93 | wax | 50 | | | |
| Seekay R123 | wax | 56.5 | | | |
| Seekay R700 | wax | 43 | | | |

addition, the water solubility of 2-chloronaphthalene has been calculated to be 6.74 mg/L [14]. It is likely that the water solubilities of most chloronaphthalenes are in the ppb range.

### 2.3.3 Spectroscopic Data

The spectral properties of chloronaphthalenes have not been extensively characterized. Two of the more complete compilations are those of Brinkman et al. dealing with ultraviolet spectra [15], and of Cencelj and Hadzi dealing with infrared spectra [16]. In both investigations 33 chloronaphthalenes were studied, although a slightly different group was chosen in each case (see Table 2-5).

2.3.3.1 Ultraviolet spectra [15]: Chloronaphthalenes, in common with aromatic hydrocarbons in general, display three $\pi$-$\pi^*$ absorption bands in the ultraviolet region above 200 nm. Brinkman et al. designated these bands $L_a$, $L_b$ and $B_b$. The $L_a$ bands, which have an intensity of about $\log \varepsilon = 4$, are correlated with a localization of two $\pi$-electrons in para-positions. The $L_b$ bands, which are sometimes hidden behind the $L_a$ bands, have intensities usually in the range $\log \varepsilon = 2$ to 3. The $B_b$ bands, the most intense in the spectrum ($\log \varepsilon = 4$ to 6), are never obscured by other transitions.

Introduction of increasing numbers of chlorine atoms in the naphthalene nucleus introduces a red-shift in the $B_b$ band. The magnitude of this shift is chiefly determined by the number of chlorine atoms and is largely unaffected by their position. The peaks of the $B_b$ bands for different degrees of chlorination are as follows: mono-, 223 to 225 nm; di-, 224 to 231 nm; tri-, 233 to 235 nm; and tetra-, 228 to 245 nm.

Changes in the $L_a$ and $L_b$ bands are more complicated that those in the $B_b$ band, being determined by both the number and position of the chlorine atoms in the naphthalene nucleus. Alpha-substitution causes a distinct bathochromic shift of the $L_a$ band; the effect of beta-substitution, which

## TABLE 2-5 Spectra of Chloronaphthalenes That Have Been Published

| Chloronaphthalene | Ultraviolet Spectra [15] | Infrared Spectra [16] |
|---|---|---|
| 1- | * | |
| 2- | * | |
| 1,2- | * | * |
| 1,3- | * | * |
| 1,4- | * | * |
| 1,5- | * | * |
| 1,6- | * | * |
| 1,7- | * | * |
| 1,8- | * | * |
| 2,3- | * | * |
| 2,6- | * | * |
| 2,7- | * | * |
| 1,2,3- | * | * |
| 1,2,4- | | * |
| 1,2,5- | * | * |
| 1,2,6- | * | * |
| 1,2,7- | * | * |
| 1,2,8- | * | * |
| 1,3,5- | | * |
| 1,3,6- | * | * |
| 1,3,7- | * | * |
| 1,3,8- | * | * |
| 1,4,5- | | * |
| 1,4,6- | * | * |
| 1,6,7- | | * |
| 1,2,3,4- | * | * |
| 1,2,3,5- | * | * |
| 1,2,4,6- | * | * |
| 1,3,5,7- | * | * |
| 1,3,5,8- | * | * |
| 1,3,6,7- | * | * |
| 1,4,5,8- | * | * |
| 1,4,6,7- | * | * |
| 1,2,3,5,7- | * | |
| 1,2,3,4,5,6,7,8- | * | |

results in an intensification of the $L_b$ band, is often obscured because of the partial overlap of the $L_b$ band by the more intense $L_a$ band.

2.3.3.2 Infrared spectra [16]: Cencelj and Hadzi obtained the spectra of the complete series of di- and trichloronaphthalenes and of nine tetrachloronaphthalenes in the spectral region between 1650 and 660 $cm^{-1}$. The investigators considered the region between 900 and 690 $cm^{-1}$ to be of greatest interest. In this region, a number of strong bands appear; these arise from the out-of-plane deformation vibrations of the hydrogen atoms attached to the naphthalene nucleus. The investigators attempted to correlate the observed bands with the number of adjacent hydrogen atoms remaining around the nucleus, but met with limited success. On the basis of the infrared spectrum of benzene, the authors suggested that a band appearing between 770 and 725 $cm^{-1}$ would be characteristic of compounds having four adjacent hydrogen atoms, and would therefore be expected to occur in all chloronaphthalenes having one ring unsubstituted. In fact, a strong band in this region was observed in all such chloronaphthalenes. It was also present, however, in 1,5-, 1,6- and 1,7-dichloronaphthalenes. The investigators expected that chloronaphthalenes containing one isolated hydrogen atom (e.g., 1,2,3- or 1,2,4-trichloronaphthalenes, 1,2,3,5-tetrachloronaphthalene) would show a band between 900 and 860 $cm^{-1}$ and this was, in fact, observed. But the band was also observed in chloronaphthalenes where no solitary hydrogen atom was present. It was concluded that the presence of a band is not a sufficient proof of the presence of the corresponding group of hydrogen atoms. The absence of a band, however, required by a certain type of substitution seems to preclude the presence of such a substitution.

### 2.3.4 Miscellaneous Physical Properties

An important parameter for the assessment of the propensity of a compound to be transported through the environment is its volatility. There do not appear, however, to be any experimentally determined vapour pressures of chloronaphthalenes reported in the literature. Dressler states that the volatilities of commercial chloronaphthalenes "range from modest to extremely low (octachloronaphthalene)" [11]. Empirical relationships do, however, exist which enable estimates of vapour pressures to be made from the boiling points of the compounds. The data presented in Table 2-6 use constants empirically derived by Driesbach [17] to provide estimates of vapour pressures of monochloronaphthalenes and some dichloronaphthalenes at ambient temperature. The vapour pressures are indeed low and dichloronaphthalenes appear to be about 10 times less volatile than monochloronaphthalenes. The volatilities of the higher chlorinated naphthalenes would be expected to be even lower.

Specific gravities of commercial chloronaphthalenes at ambient temperature range from 1.5 to 2.0. The compounds have excellent electrical resistance, with dielectric constants of 4.5±1, and direct-current resistivities of about $10^{14}$ ohm.cm at room temperature and $10^{11}$ ohm.cm at their melting points [3].

## 2.4 ANALYSIS

Chloronaphthalenes are analyzed by methods identical with, or similar to, those used for polychlorinated biphenyls and organochlorine pesticides. The most extensively used analytical technique is gas liquid chromatography (GLC), although high performance liquid chromatography (HPLC) and thin layer chromatography (TLC) have also been widely employed. Mass spectrometry and voltammetry have been less extensively used.

Chloronaphthalenes have been identified as compounds that may interfere with the analysis of organochlorine pesticides and/or polychlorinated biphenyls in environmental samples [18]. This interference, and a concern that chloronaphthalenes are undesirable environmental pollutants in their own right, has led to studies into the behaviour of chloronaphthalenes in analytical systems and to development of specific analytical techniques. An

## TABLE 2-6 Estimated Vapour Pressures (at 25°C) for Some Chloronaphthalenes*

| Chloronaphthalene | bpt. @ 101.3 kPa** | Vapour Pressure @ 25°C Pa (torr) |
|---|---|---|
| 1- | 260°C | 2.77 ($2.08 \times 10^{-2}$) |
| 2- | 256 | 3.53 ($2.65 \times 10^{-2}$) |
| 1,2- | 296 | 0.28 ($2.08 \times 10^{-3}$) |
| 1,3- | 291 | 0.41 ($3.11 \times 10^{-3}$) |
| 1,4- | 286 | 0.51 ($3.79 \times 10^{-3}$) |
| 1,7- | 285 | 0.58 ($4.32 \times 10^{-3}$) |
| 2,6- | 285 | 0.58 ($4.32 \times 10^{-3}$) |

* The vapour pressures were calculated from the Antoine equation relating vapour pressure (P) and temperature (t):

$$\text{Log } P = A - [B/(t°\text{C} + 230)]$$

and values for the Antoine constants, A and B, given in Dreisbach's Pressure-Volume-Temperature Relationships of Organic Compunds for the Cox-Chart family of naphthalene and halo-naphthalenes [17]. All that is required to use Dreisbach's empirical relationships is to know the boiling point of the compound at atmospheric pressure (101.3 kPa).

** The boiling points are those given in Table 2-3; interpolated, where necessary, to 101.3 kPa. (In cases where the pressure at which the boiling point was obtained was not reported, it was assumed that the pressure was 101.3 kPa.)

account of such techniques is presented by Brinkman and Reymer [3] in their comprehensive review of chlorinated naphthalenes.

### 2.4.1 Sample Preparation

In the mid 1970s the U.S. Environmental Protection Agency carried out extensive monitoring of chloronaphthalenes in the environment surrounding chloronaphthalene producers and users [19]. Development of sampling techniques for air, soil, and water was part of the program. Other research workers have also developed methods for environmental sampling of chloronaphthalenes.

2.4.1.1 Air samples: Erickson and co-workers developed a sampling method using polyurethane foam as the adsorbing medium for chloronaphthalenes in ambient air [19-21]. A sampling train consisting of a 12-cm diameter glass-fibre filter and two 13 x 5 cm diameter polyurethane-foam plugs housed in a glass module was used. Air was drawn through the module at a rate of about 60 L/min which gave a 24-hour sample volume of about 90 $m^3$. Chloronaphthalenes adsorbed on the polyurethane plugs were extracted with toluene and the extract evaporated to dryness. The residue was taken up in 1.0 mL hexane for analysis by GLC/MS chromatography. A sensitivity for 24-hour samples of 0.3 $ng/m^3$ chloronaphthalenes in air was reported. Prior to using, each foam plug was extracted five times at 100°C with toluene to remove potentially interfering contaminants.

Lewis and co-workers similarly suggested the use of polyurethane foam to sample pesticides, polychlorinated biphenyls and polychlorinated naphthalenes in ambient air [22]. In their method, the foam plugs (7.6 cm x 5 cm I.D.) were Soxhlet extracted with a 95:5 n-hexane:diethyl ether solution (750 mL) for 16 to 24 hours to remove the adsorbed pollutants. The extract was concentrated to 1 mL in a rotary evaporator, cleaned by column chromatography on alumina using n-hexane (10 mL) as an eluant, and the eluate analyzed by GLC.

Andersson and co-workers suggested the use of Amberlite® XAD-2 resin as the adsorption medium for determination of chloronaphthalenes in workroom air [23]. The XAD-2 resin was washed with water and methanol and extracted twice with diethyl ether in a Soxhlet apparatus overnight before use. The treated resin (150 mg) was placed in a glass tube (5 cm x 0.4 cm I.D.) with glass wool plugs at both ends. This sample tube could be used with a personal sampling pump with a capacity of about 0.2 L/min to draw air through the resin. Chloronaphthalenes adsorbed on the resin were extracted with 3 mL of diethyl ether in an ultrasonic bath for 45 minutes and the resulting solution injected directly into a GLC for analysis. The authors reported that the method was suitable for chloronaphthalene levels in air ranging from 0.001 to 5 mg/m$^3$.

Schaffernicht suggested the use of activated charcoal or sulphuric acid as adsorption/absorption media for the determination of chloronaphthalenes in workplace air [24]. Air was drawn through a sample tube containing the activated charcoal (quantity not specified) at 40 L/hour. The adsorbed chloronaphthalenes were extracted with carbon disulphide which was then evaporated to concentrate the sample prior to injection into a GLC for analysis. In the alternative method, air was drawn at 20 L/hr through 2 mL of concentrated sulphuric acid contained in a micro-impinger. Chloronaphthalenes, adsorbed in the acid, were nitrated with concentrated nitric acid and the resulting solution treated with 5 mL sodium hydroxide solution (250 g/L). A yellow colour developed which was photometrically measured at 420 nm to determine the chloronaphthalene concentration. The author reported a detection limit of about 0.5 mg/m$^3$ for chloronaphthalenes in air for both methods, but stated that the sulphuric acid/photometric method was simpler and more accurate.

2.4.1.2 Water samples: Erickson and co-workers used toluene to extract chloronaphthalenes from water samples [19,20]. The procedure involved extracting 200 mL of the water sample with three separate aliquots (25 mL) of toluene in a separatory funnel. The combined organic fraction

(75 mL) was dried over anhydrous sodium sulphate and then evaporated to dryness. The residue was taken up in 1.0 mL hexane and chromatographed on a silica-packed column using hexane as eluant. An aliquot of the hexane eluate was injected into a GLC for analysis of the chloronaphthalenes. This procedure has a sensitivity of about 200 ng/L and a mean extraction efficiency of 0.90±0.19, which was found to be independent of the pH of the water sample.

2.4.1.3 Soil and sediment samples: Erickson and co-workers used acetone and toluene to extract chloronaphthalenes from soil samples [19,20]. Soil (50 g) was allowed to stand overnight in contact with 50 mL diethyl ether to aid loosening of organic materials from the soil matrix. The diethyl ether was removed under vacuum at room temperature and the soil moistened with 5 mL water. Acetone (40 mL) was added to the soil and the mixture shaken for 20 minutes, after which time toluene (80 mL) was added and the mixture shaken for a further 10 minutes. The acetone/toluene fraction was decanted from the soil and the acetone/toluene extraction repeated twice more. The combined acetone/toluene fractions were extracted with 500 mL water. The water fraction was back extracted three times with 25 mL portions of toluene and these were added to the acetone/toluene fraction. The combined organic fraction was dried with anhydrous sodium sulphate, and then evaporated to dryness. The residue was taken up in 1.0 mL hexane and chromatographed on a silica-packed column using a hexane as eluant. The hexane eluate was analyzed for chloronaphthalenes by GLC. The method has a sensitivity of about 500 ng/kg soil.

Goerlitz and Law developed a method to extract chlorinated insecticides from suspended sediment and bottom material [25] (It was from this method that Erickson et al. developed their technique for the analysis of soil samples for chloronaphthalenes.) Although Goerlitz and Law's method was aimed at extracting chlorinated insecticides, chloronaphthalenes and polychlorinated biphenyls were also extracted. Sediment samples were filtered to recover suspended solids and bottom-material samples were centrifuged to obtain the solid component. The solid components were extracted with acetone and hexane (rather than acetone and toluene used by Erickson et al.) using a procedure similar to the above and, after column chromatographic clean-up, the extract was analyzed by GLC.

2.4.1.4 Biological samples: Erickson and co-workers simply homogenized samples of environmental biota (specifically, a small fish and a dozen apples) in an electric blender to prepare them for analysis [19]. Chloronaphthalenes in the homogenized samples were then extracted and analyzed using the same procedure as described in the preceding section for soil samples.

Takeshita and Yoshida developed a method for the extraction of chloronaphthalenes from biological samples [26]. The method was based on saponification of the sample with an ethanolic solution of potassium hydroxide, extraction of chloronaphthalenes with hexane, treatment of the extract with concentrated sulphuric acid, clean-up of the extract by silica gel column chromatography, separation from polychlorinated biphenyls by TLC on polyamide, and determination of chloronaphthalenes by GLC. These researchers used this procedure to analyze samples of human adipose tissue, obtained from cadavers, for chloronaphthalenes [27].

The use of steam distillation, or gel-permeation chromatography, or adsorption on activated carbon followed by elution with toluene to extract xenobiotic pollutants (including chloronaphthalenes) from tissue samples (fish, human seminal fluid, and human adipose tissue) is described by Dougherty and co-workers [28,29]. A number of procedures, of varied complexity, based on these three techniques and involving clean-up using chromatography and solvent extraction, produced final samples suitable for analysis by negative-chemical-ionization mass spectrometry or GLC.

Steam distillation was also used by Cooke and co-workers to extract chloronaphthalenes, polychlorinated biphenyls and DDT residues from avian tissue samples [30]. Tissue samples were blended with double distilled water (100 mL) to give a homogeneous mixture. This mixture, together with heptane (10 mL) was placed in a steam distillation unit. Cyclic steam extraction for two hours yielded a heptane extract. The unit was washed with 5 to 10 mL heptane and the washings added to the extract. Reduction of the volume to 1 mL under a nitrogen stream yielded a sample suitable for analysis by carbon skeleton gas chromatography.

### 2.4.2 Isolation and Differentiation of Chloronaphthalenes from other Organochlorine Pollutants

The large number of organochlorine compounds that may be present as pollutants in environmental samples necessitate clean-up procedures and differentiation techniques to isolate chloronaphthalenes. This is especially true for gas chromatography where it has been demonstrated that under conditions used for the analysis of organochlorine pesticide residues, commercial chloronaphthalenes exhibit peaks throughout the retention-time region of the pesticides [18]. The techniques described below are also applicable to other analytical methods.

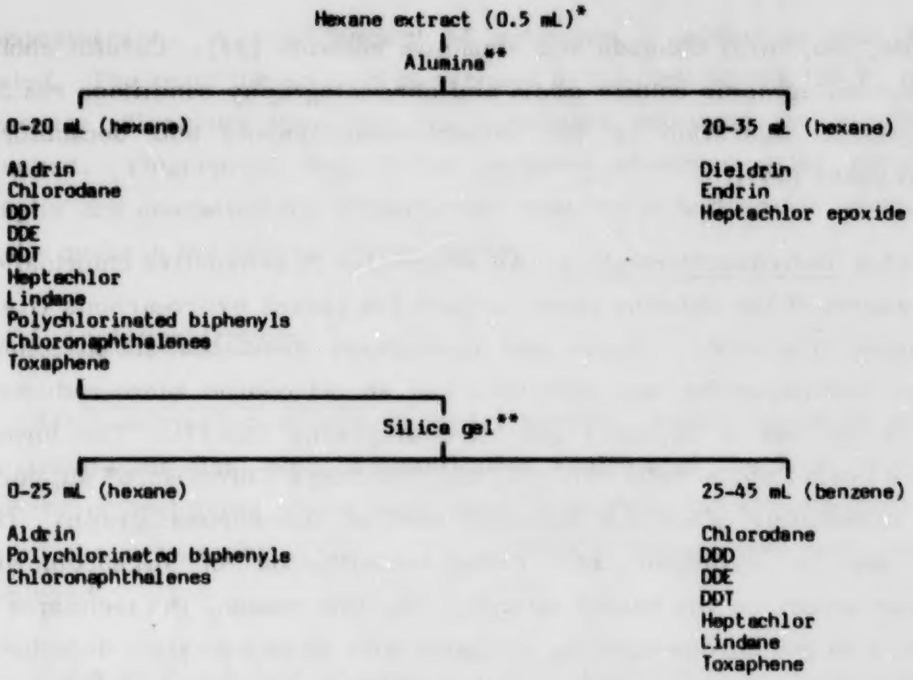
2.4.2.1 Column-chromatographic clean-up: Armour and Burke demonstrated that Halowaxes® could be separated from common organochlorine pesticides (p,p'-DDT, p,p'-TDE, and p,p'-DDE) using a silica gel column chromatographic procedure [18]. A mixture containing a Halowax® and the pesticides was loaded onto the column. Elution with 250 mL petroleum ether completely removed the Halowax® but none of the pesticides. (Polychlorinated biphenyls, if they had been present, would also have been recovered.) The pesticides could be removed by further elution with 250 mL acetonitrile-hexane-methylene chloride.

Goerlitz and Law developed a two-stage column chromatographic technique for the partial separation of a large number of organochlorine compounds in aquatic samples [25]. Two different semimicro columns, one containing alumina and the other silica gel, were employed and eluted in sequence according to the scheme shown in Figure 2-3. Chloronaphthalenes would be eluted from the silica gel column, together with polychlorinated biphenyls and Aldrin, if present.

A similar procedure to separate chloronaphthalenes and polychlorinated biphenyls from organochlorine pesticides using alumina and silica gel columns was developed by Holden and Marsden [31] and modified by Zitko [32]. The modified procedure is shown in Figure 2-4. Both chloronaphthalenes and polychlorinated biphenyls are eluted in fractions I and II; p,p'-DDE is also partially eluted in these two fractions, but separation from most other common pesticides is successful. Zitko emphasized that to achieve reproducible chromatographic conditions, the activity of the adsorbents must be carefully controlled, the activation procedures described in detail, and the quality of the solvents used for elution specified [32].

In all these clean-up procedures, chloronaphthalenes would be eluted together with polychlorinated biphenyls. If the latter compounds are present, a real likelihood with environmental samples, efforts have to be made to distinguish between the two classes of compounds.

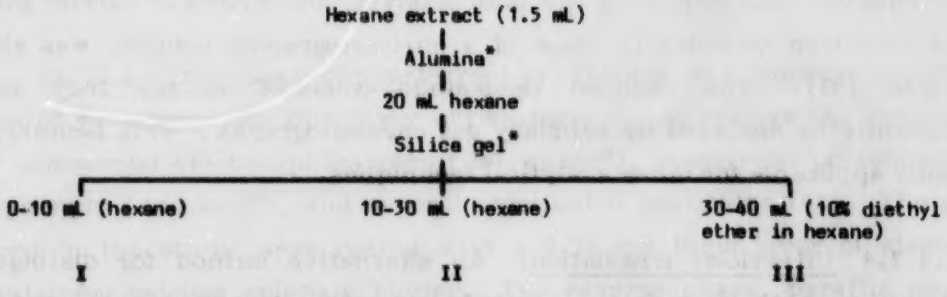
2.4.2.2 Perchlorination: To simplify the analysis of a mixture of chloronaphthalenes and polychlorinated biphenyls, conversion to single derivatives has been suggested. Hutzinger and co-workers carried out perchlorination of chloronaphthalene mixtures to yield octachloronaphthalene, by refluxing the mixture with sulphuryl chloride/antimony(V) chloride (9:1 v/v) for one hour [33]. The same researchers demonstrated that quantitative conversion of polychlorinated biphenyls to decachlorobiphenyl could be achieved by the use of antimony(V) chloride, mixtures of antimony(V) chloride and iodine and/or sulphuryl chloride, or a mixture of disulphur



* cleaned extract from environmental samples obtained by methods described in Section 2.4.1

** column bed dimensions: 8 cm x 1 cm dia.

FIGURE 2-3 Clean-up Procedure Developed by Goerlitz and Law [25]



* 2 g adsorbent in 0.7 cm dia. column

FIGURE 2-4 Clean-up Procedure Developed by Holden and Marsden [31] and Modified by Zitko [32]

**dichloride, sulphuryl chloride and aluminum chloride [33]. Careful choice of gas chromatographic column media and chromatography conditions results in successful separation of the octachloronaphthalene and decachlorobiphenyl peaks [34].**

**2.4.2.3 Dehydrochlorination: An alternative to exhaustive chlorination is the removal of the chlorine atoms to yield the parent hydrocarbons (i.e., naphthalene, biphenyl). Cooke and co-workers developed an on-column reduction technique for use with GLC and an off-column micro-reduction apparatus for use in capillary gas chromatography [35-37]. The former employs a heated noble-metal catalyst, dispersed on a Chromosorb® support, located immediately after the injection port of the chromatograph. The carrier gas is hydrogen and dehydrochlorination of organochlorine compounds occurs on the heated catalyst. For this reason, the technique is well suited to gas chromatographs equipped with flame ionization detectors, although the successful use of electron-capture and mass spectrometric detectors is also reported [36]. Reduction of chloronaphthalenes to naphthalene is quantitative for a palladium catalyst (3% Pd on Chromosorb®) at 305°C and polychlorinated biphenyls are reduced to biphenyl under similar conditions (quantitative reduction, however, was only reported for the lower-chlorine-content polychlorinated biphenyls). Alternatively, a platinum catalyst (5% Pt on Chromosorb®) at 180°C produces similar results. Nanogram quantities of the chlorinated compounds can be detected [35]. A micro-reduction unit employing the same catalysts and hydrogen carrier gas, with a cold-trap collector in place of a chromatographic column, was also developed [37]. The reduced compounds collected in the trap may subsequently be analyzed by capillary gas chromatography. This technique is equally applicable for other analytical techniques.**

**2.4.2.4 Ultraviolet irradiation: An alternative method for distinguishing chloronaphthalenes from other types of organochlorine compounds has been developed by Gulan and co-workers [38]. The technique involves individually trapping the components of the mixture as they elute from a gas**

chromatograph. A small amount of n-hexane is added to each fraction eluted. The resulting solution is exposed to the light from a 100 W, medium-pressure ultraviolet lamp and the irradiated solutions are re-chromatographed. Fingerprint degradation patterns observed after rechromatography are characteristic of particular compounds and enable identification of the peaks in the original chromatogram.

### 2.4.3 Analytical Options

After extraction of environmental samples, sample clean-up and pretreatment, the final step is quantitative analysis of the final product. A variety of techniques have been used to analyze for chloronaphthalenes, with chromatography (GLC, TLC, HPLC) being the most commonly employed.

2.4.3.1 Gas-liquid chromatography: Many GLC systems capable of analyzing for chloronaphthalenes have been developed. These systems employ a wide variety of pretreatment techniques, column compositions, chromatograph operating conditions, and detector types. Some of the systems reported in the literature are summarized in Table 2-7. Many of those in the table were developed primarily to determine organochlorine pesticides or polychlorinated biphenyls in environmental samples, but others, notably the system developed by Erickson et al. [19], were specifically for the determination of chloronaphthalenes.

2.4.3.2 Thin-layer chromatography: Stalling and Huckins report the use of reverse-phase thin-layer chromatography to resolve the components of commercial chloronaphthalenes (Halowaxes®), commercial polychlorinated biphenyls (Aroclors®), and several chlorinated pesticides [42]. The plates used in the study were coated with a 0.25 mm thick layer of kieselguhr containing calcium sulphate binder. The reverse phase, paraffin oil, was applied by soaking coated plates in an eight per cent solution of paraffin oil in petroleum ether. When the adsorbent layer had become saturated with

TABLE 2-7 Some Systems Used for the Analysis of Chloronaphthalenes by Gas-Liquid Chromatography

| Analysis | Pretreatment | Column: Dimensions | Column: Packing | Carrier Gas | Temperature | Detector | References |
|---|---|---|---|---|---|---|---|
| PCNs and dibenzofuran in PCBs | Column chromatography on Florisil | 5' x 1/8" | 10% DC-200 on Gas Chrom Q | $N_2$, 50 mL/min | 200°C | ECD | [39] |
| PCNs in analysis for organochlorine pesticides and PCBs | Column chromatography on silica gel | 6' x 4 mm | 10% DC-200 on Chromosorb W | $N_2$, 120 mL/min | 200°C | ECD | [18] |
|  |  |  | 10% DC-200: 15% QF-1 on Chromosorb W |  |  |  |  |
| PCN interference in pesticide analysis | None | 6' x 1/8" | 3% OV-101 on Gas Chrom Q | $N_2$, 37 mL/min | 180°C | ECD | [40] |
|  |  | 6' x 1/4" | 3% OV-101: 5% OV-210 on Gas Chrom Q | $N_2$, 60 mL/min | 175°C | " |  |
| Identification of PCNs in Halowaxes® | None | 10' x 1/8" | 10% Carbowax 20M on Chromosorb W | $N_2$, 30 mL/min | 180°C | ECD | [41] |
|  |  |  | 5% Bentone 34: 10% OV-101 on Supelcoport | " | " | " |  |
| Differentiation of PCNs from organochlorine insecticides and PCBs | None (two column technique with UV irradiation of column I eluate) | I: 1.2 m x 4 mm | 2% SE-30: 2% QF-1 on Anakrom ABS | 95% Ar:5% $CH_4$, 60 mL/min | 180°C | ECD | [38] |
|  |  | II: 1.2 m x 2 mm | 4% SE-30: 4% QF-1 on Anakrom ABS | $N_2$, 30 mL/min | 170 to 190°C | ECD |  |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Analysis of PCNs and PCBs in ambient air | Column chromatography on alumina | 1.83 m x 4 mm | 3% OV-1 on Gas Chrom Q | $N_2$, 60 mL/min | 180°C | ECD,<br>FID | [22] |
| PCNs in environmental samples | Column chromatography on silica gel | 1.8 m x 2 mm | 2% OV-1 on Chromosorb W | He, 30 mL/min | 150 to 230°C | MS | [19] |
| Differentiation between PCNs and PCBs | Perchlorination | 2.2 m x 2 mm | 4% OV-101 on Chromosorb W | $N_2$ or He, 30 mL/min | 260°C | ECD,<br>FID | |
| | | 1.8 m x 2 mm | 3% OV-1 on Chromosorb W | " | 250°C | " | |
| | | 1.95 m x 2 mm | 1% SE-30 on Chromosorb W | " | 220°C | " | |
| PCNs, PCBs and DDTs in environmental samples | Dehydrochlorination | n.s. | 2% RbCl on Chromosorb G | $H_2$, 40 mL/min when used with FID and ECD, 30 mL/min when used with MS | n.s. | FID<br>ECD*<br>MS | [35, 37] |
| | | n.s | 3% SE-30 on GasChrom Q | | | | |
| PCNs, PCBs and chlorophenols in workplace air | None | 1.5 m x 4 mm Chromosorb W | 1% APM on | $N_2$, 40 mL/min | 180°C for PCNs | ECD | [23] |
| Identification of PCNs in Halowaxes® | None | 2 m x 1/8" | 5% Poly MPE on Gas Chrom Z | n.s. | 150 to 250°C | FID,<br>MS | [6] |

* ECD cannot be used with RbCl column
n.s. not specified
PCNs = chloronaphthalenes, PCBs = polychlorinated biphenyls, DDTs = the DDT family of insecticides
ECD = electron capture detector, FID = flame ionization detector, MS = mass spectrometer

the solution, the plates were removed and dried. Samples of Halowaxes® (2 to 50 μL of a 1 mg/mL solution in benzene) were spotted on the plates. The plates were developed with a water-acetone-acetonitrile-methanol (5:15:40:40) solvent which had been previously saturated with paraffin oil. After drying, the developed plates were sprayed with a solution of silver nitrate in 96% ethanol (1.7 g in 200 mL), held over a steam bath for a few seconds, and placed under an ultraviolet lamp. The components appeared as dark spots on a light background. To further identify the components separated by TLC, sections corresponding to the locations of the spots were cut out of the TLC plate and extracted with diethyl ether-petroleum ether (5:95). The extract was then analyzed by GLC. The results obtained are summarized in Table 2-8.

Brinkman and co-workers report normal and reverse-phase thin-layer chromatography of a number of Halowaxes [15]. Normal TLC was carried out using a silica gel/n-hexane system, while reverse-phase TLC used Kieselguhr-G/acetonitrile-methanol-acetone-water (20:20:9:1) or Kieselguhr-G/acetonitrile-methanol-water (8:9:3) systems; the Kieselguhr-G had been impregnated with paraffin oil. Spots on the developed plates were visualized by spraying the plates with a solution of 0.5% tolidine in 80% ethanol containing 0.5% glacial acetic acid. Irradiation under ultraviolet light gave blue or blue-green, and occasionally brown, spots. From their investigations of six Halowaxes® (1000, 1001, 1099, 1013, 1014, 1051) the authors concluded that TLC is a rapid, although relatively insensitive, technique for the qualitative analysis of chloronaphthalene mixtures; reversed-phase TLC being superior to the normal technique. They also predicted that the analysis of chloronaphthalenes by reversed-phase high-performance liquid chromatography would yield excellent resolution, a prediction borne out in a subsequent paper by two of the authors (see next section).

2.4.3.3 High-performance liquid chromatography: Brinkman and co-workers describe the use of high-performance liquid chromatography to

TABLE 2-8 Detection of Chloronaphthalene Components in Halowaxes® by Reverse-Phase Thin-Layer Chromatography [42]

| Halowax® | No. of spots in TLC | GLC Analysis of Spots: Chlorine content | GLC Analysis of Spots: No. of isomers detected |
|---|---|---|---|
| 1099 | 6 | dichloro | 1 |
| | | trichloro | 2 |
| | | tetrachloro | 5 |
| | | pentachloro | 3 |
| 1013 | 7 | trichloro | 2 |
| | | tetrachloro | 5 |
| | | pentachloro | 4 |
| | | hexachloro | 3 |
| 1014 | 5 | trichloro | 2 |
| | | tetrachloro* | 2 or 3 |
| | | pentachloro* | 3 or 4 |
| | | hexachloro** | 4 or 5 |
| | | heptachloro** | 1 or 2 |

* the uncertainty in the number of tetra- and pentachloro isomers detected arises because one peak was incompletely identified by GLC and could have been either a tetra- or pentachloro isomer.

** same type of uncertainty relates to hexa- and heptachloro isomers.

identify components in several commercial chlorinated naphthalenes [15]. Chromatography was carried out on silica gel (LiChrosorb SI-60) with n-hexane, dried over molecular sieve, as the mobile phase. Components eluting from the column were detected using ultraviolet absorption at a wavelength corresponding to the absorption maximum of the commercial product. A flow rate of 1.4 mL/min at a pressure of about 8 MPa was used to elute the chloronaphthalene components and complete elution took about four minutes. The composition of Halowax 1031 determined by this method is shown in Table 2-9.

High-performance liquid chromatography was used by Brinkman and co-workers to distinguish chloronaphthalenes from polychlorinated biphenyls in commercial mixtures using perchlorination pretreatment [34]. An aluminum oxide stationary phase (LiChrosorb Alox T5) eluted with n-hexane produced better separation of the octachloronaphthalene and decachlorobiphenyl perchlorination products than did a silica gel packing (LiChrosorb RP-8). While concluding that GLC using an electron capture detector will be favoured for samples containing very low levels of chloronaphthalenes and polychlorinated biphenyls, the authors recommended HPLC instead of GLC for higher levels, pointing out that HPLC is more convenient and, with the aluminum oxide system, a more rapid technique.

Brinkman and co-workers have also demonstrated that HPLC, particularly reversed-phase HPLC, is capable of separating the highest chloronaphthalenes more effectively than GLC [43]. Halowax® 1051, which consists of 90 per cent octachloronaphthalene and 10 per cent heptachloronaphthalenes, can be separated into its three constituents -- octachloronaphthalene, 1H- and 2H-heptachloronaphthalene -- by HPLC, while GLC is incapable of separating the two heptachloro isomers. The HPLC technique used a silica gel packing (LiChrosorb RP-8 which, in the reversed-phase option, was impregnated with paraffin oil) eluted with a methanol-water solution (9-8:1-2 v/v).

TABLE 2-9 Composition of Halowax® 1031 as Determined by High-Performance Liquid Chromatography [15]

| Component | Percentage |
|---|---|
| naphthalene | < 1% |
| 1-chloronaphthalene | 75% |
| 2-chloronaphthalene | 15% |
| (1,4 + 1,5)-dichloronaphthalene | 8% |
| other chloronaphthalenes | 2% |

2.4.3.4 Mass spectrometry: In addition to its utility as a detection method for GLC, mass spectrometry may be used as a primary method for the analysis of environmental pollutants. Dougherty and co-workers have used negative-chemical-ionization mass spectrometry for the detection of xenobiotic chemicals (including chloronaphthalenes) in biological samples [28,29]. Negative chemical ionization produces simpler mass spectra of toxic compounds extracted from biological samples than the spectra obtained from positive chemical ionization or electron-impact ionization. Dougherty et al. suggested that this spectral "clean-up" occurs because, fortuitously, virtually all toxic substances are oxidizing and/or alkylating agents which are capable of readily forming negative ions in the gas phase; whereas biological molecules do not, in general, attach electrons or negative ions. Primary negative ions were generated in the mass spectrometer source by the action of 470 eV electrons on a reagent gas (isobutane or methylene chloride containing traces of oxygen). Extraction residues from biological samples were introduced into the source using a direct insertion probe. The secondary negative ions formed from the primary anions by resonance capture, dissociative capture, anion association, deprotonation, or oxygen exchange with the sample molecules were analyzed with a magnetic sector mass spectrometer.

2.4.3.5 Electrochemistry: Farwell and co-workers studied the use of voltammetry for the identification of chloronaphthalenes and other polychlorinated compounds [44]. Chloronaphthalenes, in common with other polyhaloaromatics, are irreversibly reduced at a mercury electrode, usually in a stepwise manner; the voltammetric reduction potentials of the various carbon-chlorine bonds depend on their structural positions in the parent molecule. Farwell et al. used interrupted-sweep, instead of normal, voltammetry. Their instrument permitted resolution of reduction peaks separated by less than 60 mV and characteristic reduction-potential data for 37 chloronaphthalenes (octachloronaphthalene, all the mono-, di- and trichloronaphthalenes, nine tetrachloronaphthalenes, and one pentachloronaphthalene) were obtained. Each compound gave a voltammetric fingerprint. The components of a complex chloronaphthalene mixture must first be separated by a chromatographic technique before the components can be identified by comparing the unknown fingerprint with a known standard fingerprint. At least nine micrograms of relatively pure compound are required for positive identification.

# 3. PAST AND PRESENT USES OF CHLORONAPHTHALENES IN CANADA

Information concerning the commercial uses of chloronaphthalenes in Canada appears unavailable from published sources. Considerable reliance has therefore been placed upon reported use patterns in the United States from which inferences, based on discussions with representatives of Canadian industry (see the Appendix for a list of organizations contacted), as to the situation in Canada have been drawn. The picture presented in this chapter, accordingly, is more subjective than quantitative. It does, however, provide a useful, and indeed necessary, reference point for discussions on environmental behaviour and human-health effects presented in the following two chapters.

## 3.1 BACKGROUND

### 3.1.1 Historical Perspective

The commercial use of chloronaphthalenes dates from the beginning of the twentieth century, with patents being granted for their use as impregnants for paper, wood, and fibres (U.S. Patents 914,222 and 914,223, March 2, 1909; 1,111,289, September 22, 1913: J.W. Aylsworth) [11]. During World War One chloronaphthalenes became important as protective coating materials, particularly in Germany where chloronaphthalenes were used in place of natural rubber as a protective coating material [45] and as an impregnant for paper inlays in gas masks [3]. The chemical and thermal stability of chloronaphthalenes, their low flammability, and fungus- and insect-resistant properties led to their ever-widening use into the 1950s [3,11]. Since then the use of chloronaphthalenes has steadily declined until, at present, their use is very limited; if, indeed, they are used at all.

In the 1920s and 1930s and during World War Two, chloronaphthalenes were used in the United States for heat-resistant electrical insulation in cable manufacture [11]. A number of severe occupational health problems (see Chapter 5) resulted from this activity (which used mainly penta- and hexachloronaphthalenes) such that, with a growing variety of plastics providing better alternatives, this use declined rapidly and probably ceased before the end of the 1950s [45].

During the 1940s and 1950s chloronaphthalenes were used as additives in high pressure lubricants (such lubricants were used, for example, in animal-feed pelletizing machines) and in wood preservatives. These uses were discontinued by the end of the 1950s because a number of serious cattle poisoning incidents (bovine hyperkeratosis -- see Chapter 5) had been linked to these applications [5].

The predominant uses of chloronaphthalenes (mainly, if not exclusively, commercial products containing the lower chloro-substituted naphthalenes) during the 1960s and early 1970s were as dielectrics in automobile capacitors, as engine crankcase oil additives to dissolve petroleum sludges and gums, as raw materials for the production of fabric dyes, as electroplating stop-off compounds, and as impregnants for carbon electrodes used in chlorine production [5]. But by the mid-1970s increasing costs, competing products, shifting markets and increasingly stringent industrial health and safety regulations led to a rapid decline in chloronaphthalene production and use.

### 3.1.2 Uses of Chloronaphthalenes

Industrial chloronaphthalenes were not pure materials, but mixtures of mono- and/or polychloronaphthalenes. The commercial products ranged from thin liquids to hard waxes and were manufactured in a number of countries under a variety of trade names (see Table 3-1). While it is certain that chloronaphthalenes are no longer produced as commercial products in the United States and the United Kingdom, we have no information concerning current production elsewhere, but suspect that commercial production has ceased worldwide.

TABLE 3-1 Commercial Chloronaphthalenes [11,46]

| Country | Company | Trade Name |
|---|---|---|
| United States | Halochem Inc.[a] | N-oil, N-waxes |
| | Koppers Company Inc.[b] | Halowaxes |
| United Kingdom | Imperial Chemical Industries Ltd.[c] | Seekay waxes |
| West Germany | Bayer A.G. | Nibren waxes |
| France | Prodolec | Clonocire products |
| Italy | Caffaro | Cerifal materials |

a) Halochem became the only supplier in the United States in 1977, and was identified in a recent report [46] as being the only producer in the world. At the time of writing (1982) the company no longer appears to be operational.

b) Koppers Company ceased manufacture of Halowaxes in 1977 [11].

c) Imperial Chemical Industries ceased manufacture of Seekay waxes in about 1965 [3].

NOTE: No information is available on whether chloronaphthalenes are still being produced by Bayer, Prodolec, and Caffaro.

Although chloronaphthalenes are no longer manufactured for commercial use in North America, the products and processes in which they were latterly used may still provide a potential source of environmental contamination. Accordingly, the identity, approximate composition, and major uses of commercial chloronaphthalenes reported as recently having been produced in the United States are summarized in Table 3-2. Dressler provides a more detailed breakdown of their uses [11]:

> Monochloronaphthalenes and mixtures of mono- and dichloronaphthalenes have been used or recommended for chemical-resistant gage fluids and instrument seals, as heat exchange fluids, high boiling specialty solvents, for colour dispersions, as engine crank case additives to dissolve sludges and gums, and as ingredients in motor tuneup compounds. Monochloronaphthalene has been used as a raw material for dyes and as a wood preservative with fungicidal and insecticidal properties, although the latter application is no longer practised in the United States.
>
> The tri- and higher-chlorinated naphthalene products have been used as impregnants for condensers and capacitors and dipping/encapsulating compounds in electronic and automotive applications; as temporary binders in the manufacture of ceramic components; in paper coating and impregnation; in precision casting of alloys; in electroplating stop-off compounds; as additives in gear oils and cutting compounds; in flameproofing and insulation of electrical cable and conductors (e.g., as bitumen blends); as moisture-proof sealants; and as separators in batteries. Technical octachloronaphthalene has been recommended as an additive in grinding-wheel media and cutting-oil coolants. Blends of polychloronaphthalenes with polyisobutylenes are used as masking compounds in electroplating.

In addition to these uses, the compounds are, have been, or may be used for a diversity of applications.

Dichloronaphthalene is potentially useful as a starting material for poly(arylene sulphides) by reaction with sulphur and soda ash [47]. A U.S. patent describes the reaction of octachloronaphthalene with sodium hydroxide in dimethyl sulphoxide to give heptachloro-1-naphthol, a compound claimed to be useful as a fungicide, algicide, and bactericide [48]. Another, and recent, U.S. patent describes the use of dichloronaphthalene (or dichlorobenzene) containing hydroperoxides as a fuel-oil additive, with the claim that combustion will be improved [49]. Octachloronaphthalenes

## TABLE 3-2 Characteristics of Commercial Chloronaphthalenes Recently (c. 1977) Manufactured in the United States [46]

| Company Products | | Chlorine | Approximate | |
|---|---|---|---|---|
| Halochem | Koppers | Content | Composition | Uses |
| Monochloro-naphthalene | Halowax 1031 | 22% | 95% mono<br>5% di | Engine oil additives; proprietary uses in fabric |
| N-Oil 12 | Halowax 1000[a] | 26% | 70% mono<br>30% di | Engine oil additives; proprietary uses in fabrics |
| N-Wax 34<br>(and 34S) | Halowax 1001[b]<br>(and 1001S) | 50% | 7% di<br>30% tri<br>63% tetra | Dielectric impregnants in automotive capacitors |
| N-Wax 43<br>(and 43B) | Halowax 1099[b]<br>(and 1099B) | 52% | 2% di<br>15% tri<br>83% tetra | Dielectric impregnants in automotive capacitors |
| N-Wax 45 | Halowax 1013 | 56% | 10% tri<br>50% tetra<br>40% penta | Electroplating stop-off compounds; impregnants in carbon electrodes used for chlorine production |
| N-Wax 56<br>(and 56B) | Halowax 1014 | 62% | 20% tetra<br>40% penta<br>40% hexa | Electroplating stop-off compounds; impregnants in carbon electrodes used for chlorine production |
| N-Wax 80 | Hallowax 1051 | 70% | 10% hepta<br>90% octa | Unknown |

NOTE: In 1972 the following compositions of these compounds were reported by Koppers Company (as outlined in the report by Kover [5]):

a) 60% mono
40% di

b) 10% di
40% tri
40% tetra
10% penta

fused with sulphur at 315 to 400°C yields a tetrachloronaphtho-bis-dithiole which can be used as a yellow colourant in plastics [50]. Monochloronaphthalene may be used as a solvent in the polymerization of polyacrylates and, at the same time, confers a stabilizing effect on the polymer during the polymerization reaction [51].

There are, in addition, purely laboratory uses of the compounds. For example, the concentration of oil in the flesh of avocados is used as a regulatory criterion of the maturity of the fruit, and 1-chloronaphthalene is used as the solvent for the extraction of the avocado oil [52]. The change in chemical shifts in high-resolution nuclear magnetic resonance spectroscopy of poly(methyl methacrylates) when going from deuterated chloroform as the solvent to an aromatic solvent such as deuterated 1-chloronaphthalene, yields information on the sterochemical behaviour of the polymer in solution [53]. Investigations of homogenous liquid-phase catalysis on inert support media (e.g., alumina) have employed 1-chloronaphthalene as a model compound for the liquid phase, and it was suggested that this compound may be the preferred catalyst-carrier for the isomerization of quadricyclene to norbornadiene [54]. Monochloronaphthalene (the 1-chloro isomer) has also been used in photochemical systems; as an aid to the study of the second triplet state of naphthalene [55], and as a compound capable of Q-switching a ruby laser [56]. (This latter phenomenon is thought to arise from an enhancement of reflectivity of the liquid, during the evolution of the laser pulse, through the formation of a periodic refractive index modulation in the liquid by the action of standing waves [56].)

The above listing of examples of the use of chloronaphthalenes does not, of course, imply increased commercial use of the compounds in the future. But it does present an illustration of the diversity of their minor applications.

### 3.1.3 The Production of Chloronaphthalenes in the Recent Past

The production of and market for chloronaphthalenes have not been well documented. The most complete picture available is provided by studies into environmental health aspects of chloronaphthalenes carried out by the U.S. Environmental Protection Agency [5,45,46]. The data concerning production of chloronaphthalenes in the United States over the past 25 years presented in Table 3-3 were obtained from information provided in these reports.

It is clear from the table that production of chloronaphthalenes in the United States dropped dramatically in the mid-1970s. A similar drop probably occurred in other countries. For instance, it was reported that production of chloronaphthalenes in West Germany in 1972 was about 75 000 tonnes (considerably in excess of production in the United States) [57]. However, a more recent publication suggests that "the present (1976) total world market for PCNs (polychlorinated naphthalenes) has been estimated at '... probably less than 800 tons'" [58]. This decline likely correlates with the dramatic drop in production and use of polychlorinated biphenyls (which were used in much larger quantities than, and in analagous ways to, chloronaphthalenes [5]) in the same time period, occasioned by fears of severe health effects and consequent stringent regulations by most countries. Canada, for example, banned the use of polychlorinated biphenyls in 1977 for all but a few strictly specified and regulated uses [59].

The only detailed breakdown of the market for chlorinated naphthalenes is that provided to the U.S. Environmental Protection Agency by Koppers Company for the 1972 United States market [5]. As may be seen from Table 3-4, the largest market (65 to 66 per cent) was for dielectrics used in automobile capacitors, with lesser uses as engine oil additives, for the manufacture of proprietary fabric dyes, and in electroplating stop-off compounds.

## TABLE 3-3 Production of Chloronaphthalenes in the United States

| Year | Total Production | Degree of Chlorination mono- | di-,tri-,tetra- | higher* | Reference | Comments |
|---|---|---|---|---|---|---|
| 1956 | 3200 t | - - - - not available - - - - - | | | [5] | |
| 1972 | < 2270 t | < 457 t | < 1551 t | < 262 t | [5,46] | Data estimated from information provided in the references indicated, which in turn was supplied by the Koppers Company |
| 1978 | < 68 t | < 22 t | < 45 t | < 1 t | [45] | Data obtained from Halochem** by the EPA |
| 1979 | < 270 t | < 54 t | < 203 t | < 13 t | [45] | Estimates of the projected market for 1979, provided by Halochem** to the EPA |

* mainly pentachloronaphthalenes

** a company that appears to be no longer in existence

## TABLE 3-4 Uses of Chlorinated Naphthalenes in the United States in 1972 [5]

| Halowax | % of Chlorinated Isomers | % Market* (1972) | Uses |
|---|---|---|---|
| 1000 | 60% mono 40% di | 15-18% | Engine oil additive to dissolve |
| 1031 | 95% mono 5% di | | sludge and deposits |
| 1000 | 60% mono 40% di | 10% | Proprietary uses in |
| 1031 | 95% mono 5% di | | fabric |
| 1001 | 10% di 40% tri | 65-66% | Impregnant for automobile |
| 1099 | 40% tetra 10% penta | | capacitors |
| 1013 | 10% tri 50% tetra 40% penta | 8% | Mostly as electroplating stopoff |
| 1014 | 20% tetra 40% penta 40% hexa | | compounds, also impregnant for electrodes used in chlorine production |
| 1051 | 10% hepta 90% octa | 0.5% | Unknown |

* based on market of less than $2.27 \times 10^9$ g (5 million lbs)

## 3.2 CHLORONAPHTHALENE USE IN CANADA

In 1980, a notice appeared in the Canada Gazette requiring all companies in Canada that manufactured, imported, used or sold chloronaphthalenes in quantities greater than 1 kg in 1979, or who planned to do so in 1980 and/or 1981, to report such amounts to the Environmental Protection Service of Environment Canada [60]. No such reports were made, and a follow-up survey of 350 chemical companies by the Department produced a similarly negative result [61]. Clearly, chloronaphthalenes *per se* are neither used nor produced in commercial quantities in Canada at present. In addition, we are informed by federal government officials that, at least since 1970, chloronaphthalenes have not been imported as identifiable chemicals in sufficiently large quantities to merit a separate import registration category [63]. Furthermore, to our knowledge, chloronaphthalenes have never been manufactured in Canada -- or at least, not in the last 20 years or so. It is reasonable, therefore, to suppose that chloronaphthalenes entered Canada largely as "hidden imports" (i.e., as part of finished products) in unidentified, and probably small, quantities.

To gain a general idea of the amounts of chloronaphthalenes that may have existed in products used in Canada, it must be assumed that uses extant in the United States were also common to this country. A further assumption, that the Canadian market was some 10 per cent of that of the United States, leads to the situation presented in Table 3-5. A substantial portion of the less than 227 tonnes estimated as entering Canada in 1972 would likely have been imported as finished or semi-finished products. By 1978, the total quantity of chloronaphthalenes coming into Canada would have declined to less than seven tonnes and now (1982) there appears to be little or none. The responses received from representatives of Canadian industry, presented below, serve to complement this scanty picture of chloronaphthalenes in Canada.

TABLE 3-5 Estimated Yearly Amounts of Chloronaphthalenes Used in Canada*

| Uses | Year<br>1972 | <br>1978 | <br>1982 |
|---|---|---|---|
| In automobile capacitors: | < 150 t | n/a | none |
| In engine oils: | < 37 t | n/a | none |
| In fabric dyes: | < 22 t | n/a | none |
| In electroplating stop-off compounds: | < 17 t | n/a | none |
| Unknown: | < 1 t | n/a | none |
| TOTAL AMOUNT | < 227 t | < 7 t | none |

* estimated as 10 per cent of the amounts used in the United States (from data presented in Tables 3-3 and 3-4).

n/a information on which to base an estimate is unavailable.

A representative of General Motors Canada informed us that chloronaphthalenes were used in their automotive capacitors until the early 1970s. After this time the chloronaphthalene impregnated paper dielectric was replaced by a Mylar® film. (The chloronaphthalene impregnated capacitors were manufactured in the United States.) It was also stated that the use of chloronaphthalenes as a crankcase oil-additive was discontinued some 10 to 15 years ago because the compounds were found to cause carbon deposits which led to sticking of valves and piston rings. General Motors have never used chloronaphthalenes in their gear oils [63].

Chloronaphthalenes were never used in power capacitors, which had used polychlorinated biphenyls but now use isopropyl biphenyls. A representative of a Canadian manufacturer of small capacitors (e.g., those used as starters for electric motors and fluorescent lights) said that they never used chloronaphthalenes as an impregnant in their paper capacitors but rather used a mineral oil [64].

A representative of Dow Chemical Canada Inc. reports that the carbon anodes used in their chlorine manufacturing facility are imported from the United States and do not currently contain chloronaphthalenes. Dow's representative did not know whether the anodes had contained chloronaphthalenes in the past [65].

Fabric dyes are not manufactured in Canada (pigments, however, are) [66]. Fabric-dye preparations, which may have contained chloronaphthalenes in the past, would have been imported.

Finally, two of Canada's largest suppliers of commercial chemicals do not carry any chloronaphthalenes in their catalogues. One representative stated that his company had not carried these compounds in the 25 years he had been with the company [67].

# 4. CHLORONAPHTHALENES IN THE ENVIRONMENT

Very little systematic work has been carried out on the release, subsequent transport and eventual fate of chloronaphthalenes in the environment, and only fragmentary information exists. Chloronaphthalenes have, however, been detected in environmental samples -- in biota, in soils and aquatic sediments, and in the atmosphere surrounding chloronaphthalene manufacturing facilities. To provide an idea of the extent to which the Canadian population might be affected requires a knowledge of where the compounds might most likely be found and how long they might be expected to persist.

## 4.1 SOURCES

The largest use of chloronaphthalenes in the 1970s was as a dielectric in small capacitors, particularly those in automotive ignition systems. Since such capacitors are commonly changed whenever an automobile engine is tuned, solid waste disposal sites may well have become a minor reservoir of chloronaphthalenes. Effluents from facilities involved in textile dying and electroplating processes may also have contained chloronaphthalenes and thus the compounds may have been introduced in sewage sludge.

Laboratory experiments have shown that chloronaphthalenes may be formed from naphthalene (an observed aquatic pollutant) under conditions similar to those used to disinfect drinking water and wastewater, and this observation has led to speculation that water treatment activities may be a continuing source of chloronaphthalenes in the environment [68]. In the experiments, aqueous solutions containing 10 ppm or 500 ppm of napthalene, with the pH adjusted with hydrochloric acid, were treated with sodium hypochlorite at room temperature. Both the amount of naphthalene chlorinated and the extent of chlorination were found to increase as the pH of the test solution was decreased.

Trace quantities of chloronaphthalenes have been reported in fly-ash samples taken from municipal incinerators located in major urban centres in Canada (southern Ontario), The Netherlands and Japan [69]. The report gave neither indication of the amounts of chloronaphthalenes recovered nor of the source of the substances. (Mono-, penta-, and hexachloronaphthalenes were among an extremely large number of organic compounds found.)

Chloronaphthalenes have also been identified as contaminants in commercial polychlorinated biphenyls (PCBs) [39,70]. The amounts found, however, were very small (less than about 0.05 mole per cent in one study [70]). Because of the widespread environmental distribution of PCBs and their continued if restricted use, PCBs may be considered as a current environmental source of chloronaphthalenes. Indeed, human tissue samples in which PCBs were detected were also found to contain trace quantities of chloronaphthalenes (v. infra).

## 4.2 LEVELS FOUND IN THE ENVIRONMENT

As pointed out in Chapter 2, analytical techniques capable of separately identifying chloronaphthalenes from among other chlorinated organic pollutants (e.g., organochlorine pesticides, polychlorinated biphenyls) have only been developed in the last decade. This time period also coincided with a dramatic reduction in the use of the compounds. Little systematic monitoring of chloronaphthalenes has been carried out and much of the available data on their environmental levels stems from surveys of the dispersion of other organochlorine pollutants, notably polychlorinated biphenyls.

### 4.2.1 Levels Found Close to Identified Sources

In 1976 the U.S. Environmental Protection Agency commissioned a survey of levels of chloronaphthalenes in terrestrial and biological samples obtained in the vicinities of the only U.S. producer and some of the more important users of the compounds (notably capacitor manufacturers) [19].

The major results of this survey are presented in Table 4-1. The samples were obtained from locations along the arms of orthogonal transects of the plant site, and ranged to as far as two or three kilometres from the facility. The chloronaphthalenes contained in the samples were analyzed using gas chromatographic/mass spectrometric methods. (Details of the analytical techniques used in the survey have already been described in Section 2.4.)

Air concentrations (occasionally higher than 1 $\mu g/m^3$) were determined from samples collected over a 24-hour period. The levels obtained were very dependent on the wind speed and direction. Soil samples (5 cm diameter, 15 to 20 cm long) were taken at two locations (one "near" and one "far") along each arm of the transects. In addition, grab soil samples were collected at locations suspected of contamination, such as sanitary landfills and dumps. Concentrations ranging from non-detectable to greater than 1 ppb were found. Water samples were collected upstream and downstream as 24-hour composite samples or, where appropriate, as single grab samples. Concentrations ranging from non-detectable to ppb quantities were found.

As might have been expected, levels of chloronaphthalenes from samples collected in the vicinity of the chloronaphthalene producer were generally considerably higher than those found in the vicinity of chloronaphthalene users.

In addition to the extensive sampling of the atmospheric, terrestrial and aquatic environments, two samples of biota (a dead fish and some apples) found in the vicinity of the chloronaphthalene producer were analyzed and found to be contaminated with chloronaphthalenes. No attempt was made to ensure that the samples were representative of biota in general. The presence of the compounds indicates, however, that chloronaphthalenes may well enter the food chain as environmental pollutants.

## TABLE 4-1 Environmental Levels Found Near One Chloronaphthalene Producer and Two Users in the United States [19,20]

| Location | Sample | Average Levels (range) | Comments |
|---|---|---|---|
| Koppers | air | 150 (25 to 450) ng/m$^3$<br>1400 (120 to 2900) ng/m$^3$ | Sampling carried out on two separate days. Results very dependent on wind speed and direction. |
| | soil | 940 (130 to 2300) µg/kg | One soil sampling site said to be an old waste dump of Koppers. |
| | water | trace | Detection limit, 0.2 µg/L |
| | fish | 39 µg/kg | The sample was a dead fish taken from a stream near the plant. It is unknown whether the PCNs detected had been ingested or were absorbed before or after death. |
| | apples | 90 µg/kg | The sample, approximately one dozen apples, was collected from the ground surrounding a farm approximately 1 km from the plant. |
| General Electric | air | 3.1 (n.d. to 7.3) ng/m$^3$<br>1.2 (n.d. to 3.9) ng/m$^3$ | Sampling carried out on two separate days. Results very dependent on wind speed and direction. |
| | soil | 2 (n.d. to 7.3) µg/kg | Three to five samples from each of eight sites. |
| | water | 0.6 µg/L<br>5.5 µg/L | Two samples taken, one upstream and one downstream. |
| Cornell Dublier | air | 19 (9.8 to 31) ng/m$^3$<br>17 (9.8 to 33) ng/m$^3$ | One sample from each of two separate days. |
| | soil | 240 (n.d. to 470) µg/kg | Three samples from each of eight sites. |
| | water | n.d.<br>0.6 µg/L | Two samples taken, one upstream and one downstream. |

n.d. not detectable: detection limits are 0.3 ng/m3 for air, 0.5 µg/kg for soil, and 0.2 µg/L for water.

Sites: Koppers Chemical and Coatings Company, Bridgeville, PA.
General Electric Company, Fort Edward, NY.
Cornell Dublier Electronics Company, Sanford, NC.

Note: The detailed sampling protocol and analyticial results are presented in reference [19]; the levels and ranges given in the table are those provided by the authors in reference [20]. In general, the chloronaphthalene levels found decreased with distance from the facilities. Sampling was carried out in 1976.

### 4.2.2 Levels Found in the General Environment

In contrast to the large body of information on the dispersion of polychlorinated biphenyls throughout the world environment, this type of data is sparse for chloronaphthalenes. Nonetheless, as may be seen from Table 4-2, chloronaphthalenes have been detected, at concentrations in the low ppb range, in many parts of the world. In most cases, chloronaphthalenes were found associated with, but in significantly lower concentrations than, polychlorinated biphenyls.

## 4.3 ENVIRONMENTAL TRANSPORT AND FATE

The data presented in the previous section have shown that chloronaphthalenes were released into the environment and that they have the potential to become dispersed. These data are observational in nature and information on which to model and predict the behaviour of chloronaphthalenes in the environment is mostly lacking. Such information as does exist, however, concerning the transport, degradation and fate of chloronaphthalenes in the environment is presented below.

### 4.3.1 Transport

The properties that made chloronaphthalenes useful as commercial products -- stability and negligible water solubility -- also mitigate their rapid dispersion. Neglecting the aspect of bulk transport by biota (a theoretical possibility but, given the low environmental concentrations of chloronaphthalenes, one of negligible significance), chloronaphthalenes will be transported within the atmospheric and aquatic systems, with potential exchange of the compounds between the two.

4.3.1.1 Atmospheric dispersion: At room temperature, chloronaphthalenes have low volatility which decreases with the degree of chlorination [5]. Chloronaphthalene vapours, however, have been known to

TABLE 4-2 Summary of Levels of Chloronaphthalenes Found in the General Environment

**TERRESTRIAL SAMPLES**

| Year | Site | Type of Sample | Level | Comments | References |
|---|---|---|---|---|---|
| 1972 | Drainage ditch (south Florida, USA) | sediment<br>water | 1,250 to 5000 µg/kg<br>5.7 µg/L | A mixture of PCNs was found. The source of contamination was suspected as being a nearby aircraft overhaul hangar. | [5,71] |
| 1974 | Guadalupe River (San Francisco Bay, USA) | sediment | 55 µg/kg | 26 sites in the San Francisco Bay area were tested for chlorinated hydrocarbons. This was the only site where PCNs were found and their concentration was such that the chromatographic peak for PCBs was obscured by the PCN peak. | [72] |
| 1976 | Japan (location not specified) | sediment | detected | Samples obtained from the surroundings of a "reproduction factory of used transformer oil". No detection limits were quoted, merely, "a very small quantity of PCN residues in sediments". | [73] |
| 1979 | Lake Michigan (Waukegan, IL, USA) | sediment | detected | No detection limits were quoted. Penta- and hexachloronaphthalenes were the only PCNs detected. | [74] |
| 1979 | Severn River (UK) | sediment | *** | Limit of detection for PCNs was approx. 200 ppb. | [75] |

BIOLOGICAL SAMPLES

| | | | | | |
|---|---|---|---|---|---|
| 1970 to 1977 | Various inland waterways in USA | Fish tissue | detected | 13 samples from a variety of freshwater fish species. All contained PCNs, tetra- to hexachloronaphthalenes found. | [29,74] |
| 1979 | Hudson River (New York, USA) | Turtle | detected | Pentachloronaphthalene was the only PCN found. | [29,74] |
| 1979 | Baltic Sea | Seal | *** | Limit of detection not stated. | [29,74] |
| 1975 to 1976 | Tyrrenian coast of Italy | Seagulls liver: | 62,500 ppb,<br>700 ppb | PCNs found in 2 out of 5 seagulls. Of the three storage compartments analyzed (adipose tissue, liver, plumage), PCNs were only found in the liver. Levels expressed on a wet-weight tissue basis. | [76] |
| 1980 | Southwest England | Birds of prey<br>liver:<br>muscle:<br>kidney: | <br>30 to 510 ppb<br>40 to 490 ppb<br>340 to 1500 ppb | Levels are quoted on a dry-weight tissue basis. Three species were sampled: kestrels (5), sparrow hawk (1), barn owl (1). | [30] |
| 1979 | Japan (location unspecified) | Humans adipose tissue: | 2.8 to 16.9 ppb | Tissue samples from 10 cadavers of individuals (8 male, 2 female) ranging from 25 to 73 years of age. Tri- to hexachloronaphthalenes found. | [27] |
| 1981 | United States | Mother's milk: | *** | Limit of detection 20 to 100 ppb | [77] |

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*** Chloronaphthalenes were analyzed for, but none were detected at the detection limits specified.

contaminate ambient air as a result of manufacturing processes using the hot compounds and have, incidentally, caused occupationally-related disease (see Chapter 5). Ventilation in such occupational environments would have expelled the vapours to the outside air. Because chloronaphthalenes are solids at ambient temperatures (or a liquid of low volatility in the case of 1-chloronaphthalene) the compounds would have been transported as finely divided particles. In a global sense, therefore, atmospheric dispersion from terrestrial point sources would be a strictly local phenomenon.

4.3.1.2 Transport by water: Chloronaphthalenes are reported as having very low water solubilities [5] and, as discussed in Section 2.3.2, the majority likely have solubilities in the ppb range. They are, however, soluble in most organic solvents and it has been speculated that chloronaphthalenes would be more readily adsorbed by organic-containing particulates in natural water and that adsorption could be an important transport process [14]. This supposition would appear to be supported by the data presented in Tables 4-1 and 4-2 which indicate that the majority of chloronaphthalenes detected in aquatic samples were in sediments, although this may have resulted only because chloronaphthalenes are more dense than water. Erickson and co-workers have claimed that their results on environmental sampling in the vicinity of chloronaphthalene producers and users (see Table 4-1) suggested that transport of chloronaphthalenes by water over any significant distance was slight and was a reasonable conclusion in light of the low solubility of the compounds [19].

A number of models have been developed to explain the observed rapid disappearance by volatilization of organic pollutants of low vapour pressure and low water solubility (notably DDT) from water bodies [78-80]. Although the mechanistic explanation of how these models function (the principle of "codistillation") has been suggested as being incorrect [81], the essentially empirically derived formulae have been used with some success as predictive tools for the transport of sparingly soluble pollutants from water bodies to the atmosphere. To use such formulae, however, it is necessary to know the water solubility and vapour pressure of the pollutant -- data that are lacking for chloronaphthalenes. Little can therefore be said regarding transfer functions of chloronaphthalenes from water to the atmosphere, except analogy with other water insoluble pollutants suggests that this transfer would probably occur. A laboratory experiment using 2,2'-dichlorobiphenyl, a compound similar to chloronaphthalenes, showed that about 20 per cent of the biphenyl (initial concentration, 98 ppb) was removed from water at 0 to 2°C when in the presence of air at 25°C and 36 per cent relative humidity [81]. Data of this type indicate that transfer might happen under environmental conditions.

### 4.3.2 Degradation

Chloronaphthalenes are physically stable and chemically unreactive. The compounds are resistant to most acids and alkalies, and are not readily dechlorinated [5]. Chloronaphthalenes in the environment would, therefore, be expected to be relatively persistent. There are, however, few studies which document the characteristics of environmental degradation, and the probable environmental behaviour of the compounds has to be deduced largely from laboratory studies of their reactions.

4.3.2.1 Hydrolysis: Chloronaphthalenes would not be expected to hydrolyze in water, particularly within the pH range encountered in natural water bodies. Attack by hydrogen or hydroxyl ions under the mild conditions in the environment would not occur because of the aromatic stability of the naphthalene nucleus.

4.3.2.2 Photolysis: Chloronaphthalenes exhibit moderate absorption in the 300 nm region and photochemical reactions within this region have been extensively studied by Ruzo and co-workers [82-84].

In methanol solution, for example, dechlorination and dimerization were the major reactions, while small amounts (< 2%) of methoxylated naphthalenes were also detected [82]. The wide variation in dechlorination-product/binaphthyl ratios observed among the mono-, di-, tri- and tetrachloronaphthalenes indicated marked substituent effects. In general, those chloronaphthalenes with vicinal or peri substitution gave larger amounts of dechlorinated products, while unhindered chloronaphthalenes gave mostly dimers. Thus, 1,8-dichloronaphthalene showed an unusually high proportion of dechlorination product and a large relative reaction rate (about nine times that of the 1,4-isomer). Correspondingly, 1,3,5,8-tetrachloronaphthalene was more reactive than its 1,2,3,4-analog by a similar factor. The authors suggested that both electronic and steric factors influence the reaction rates and products observed. The 1,8-dichloro compound is one of the few chloronaphthalenes for which stabilization of the triplet diradical (formed as the initial product of photolysis) over both chlorine atoms is not possible. The increased possibility for resonance stabilization of the triplet biradical in the higher chlorinated compounds was postulated as the reason for the slower reactions observed for the more highly chlorinated species.

In aqueous acetonitrile, a solvent which may be considered a suitable model system for environmental photochemistry, the main photo-products from 1-chloronaphthalene were chlorobiphenyl, 1-naphthol, and a hydroxylated dimer [83]. In the presence of oxygen, dimer formation was largely suppressed and the naphthol was the major product. In a study to identify the mechanism of this photolysis, it was demonstrated, that in the presence of electron donors (triethylamine and 1,3-cyclohexadiene), the photoreduction of 1-chloronaphthalene to naphthalene was stimulated and occurred by a charge transfer mechanism. But, in the absence of such electron donors, 1-chloronaphthalene itself acts as a donor molecule leading to biaryl formation through the formation of eximers [84].

Irradiation of 2,3-dichloronaphthalene in methanol by sunlight has been shown to yield the same products as those formed by 300 nm photolysis [82]. In addition, sunlight irradiations of Halowax 1014, 1,5-dichloronaphthalene and 2-chloronaphthalene as solid films on quartz gave only polymeric material insoluble in organic solvents. It was suggested that the formation of polymeric material was not surprising in the light of the solution photochemistry clearly indicating the facile generation of radicals [82].

In summary, these researchers suggest that photochemical reactions have been shown to be a minor degradation pathway in the environment, because solar radiation of the wavelengths required is present in the ecosystem [85]. The authors have further suggested that environmental degradation of chloronaphthalenes through photochemical pathways may prove more efficient than biological degradation [82].

4.3.2.3 Biodegradation: Only monochloronaphthalenes have been investigated with regard to environmental degradation by biological organisms [86,87]. The only organisms used in these studies were bacteria.

The metabolism of 1-chloronaphthalene by two species of naphthalene-utilizing bacteria isolated from soil has been investigated [86]. The bacteria were grown in a mineral salts medium at pH 6.9, with 1-chloronaphthalene added as the sole source of organic carbon. Two metabolites were isolated: 8-chloro-1,2-dihydro-1,2-dihydroxynaphthalene and 3-chlorosalicylic acid. These metabolites demonstrated that the initial site of bacterial degradation is the ring which does not contain the chlorine substituent (see Figure 4-1).

The rate of metabolism of organochlorine pollutants (including 1- and 2-chloronaphthalene) was assessed using sewage sludge [87]. The bacteria in the sewage sludge were first activated by treating with the appropriate non-chlorine-substituted parent hydrocarbon (i.e., naphthalene in the case of the monochloronaphthalenes). The purpose was to develop, in each case, strains of bacteria capable of assimilating the various classes of organochlorine pollutants. The activated sludge was then added to aqueous solutions containing inorganic nutrients and each of the test compounds or the parent hydrocarbons (at concentrations of 1 mg/L) as the sole carbon

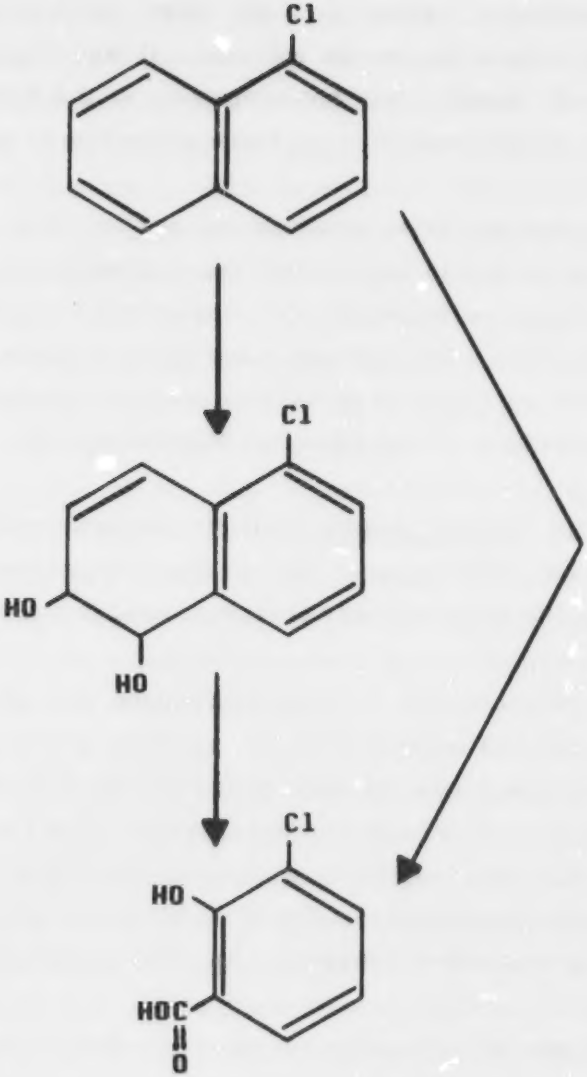

FIGURE 4-1 Suggested Route of Decomposition of 1-Chloronaphthalene by Soil Bacteria*

* Adapted from a diagram presented by Kover [5]

source. The metabolism of the organic substrate was followed by measuring the change of chemical oxygen demand of the system with time. It was demonstrated that naphthalene was much more readily metabolized than either 1- or 2-chloronaphthalene, and 2-chloronaphthalene was metabolized slightly faster than 1-chloronaphthalene. Similar tests showed that while benzene was metabolized at a similar rate to naphthalene, chlorobenzenes (1-chlorobenzene and 1,2,4-trichlorobenzene) were metabolized very much more slowly than the chloronaphthalenes. The trichlorobenzene, in turn, was found to be more slowly metabolized than monochlorobenzene.

Results from these two studies of microbial degradation suggest that: 1) chlorinated naphthalenes are more resistant to biodegradation than naphthalene (a readily biodegradable compound); 2) the higher the degree of chlorination, the more slowly chloronaphthalenes will be biodegraded; and 3) chloronaphthalenes containing chlorosubstituents in both rings may be more resistant to biodegradation than chloronaphthalenes containing chlorine in only one ring. It is also probably safe to speculate that chloronaphthalenes, like other organochlorine pollutants, will be comparatively resistant to environmental biodegradation.

### 4.3.3 Environmental Sinks

The low water solubility of chloronaphthalenes coupled with their solubility in most organic solvents suggest that the compounds would tend to concentrate in soils and sediments. Assuming that biotransfer occurs, bioconcentration of chloronaphthalenes may also be expected. There are, however, no studies which have systematically quantified such concentration effects.

One physical parameter used to predict environmental concentration of organic pollutants is the octanol/water partition coefficient. Unfortunately, experimentally measured octanol/water partition coefficients for chloronaphthalenes have not been reported in the literature. Octanol/water partition coefficients have, however, been calculated for chloronaphthalenes and values ranging from about $10^4$ for monochloronaphthalenes to about $10^9$ for octachloronaphthalene have been predicted [45].* Such values indicate a moderate ability of the compounds to concentrate in soils and sediments, and in biota.

The environmental monitoring data presented in Tables 4-1 and 4-2, do indeed show a tendency for the compounds to concentrate in sediments and in biota. But much more extensive and systematic studies, both in the laboratory and in the field, would be required to quantitatively identify the behaviour of chloronaphthalenes in these potential environmental sinks. Given that the compounds appear to be no longer used in Canada, such studies may be of more academic than practical use.

## 4.4 EXPOSURE OF CANADIANS TO CHLORONAPHTHALENES

The discussions presented in this chapter and in the previous chapter suggest that exposure of the Canadian population to chloronaphthalenes is extremely low at the present time -- the compounds appear to be used no longer, their transport is limited, and environmental degradation (albeit at a slow rate) may occur by photolytic and biological action. However, limited environmental monitoring showing the presence of chloronaphthalenes in some biota indicate that the compounds may have entered the human food chain and calculated octanol/water partition coefficients suggest that the compounds might bioaccumulate. Nonetheless, the data are totally inadequate to predict quantitatively the uptake of chloronaphthalenes in humans from environmental sources.

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* It must be noted that these values were predicted, by interpolation, from octanol/water partition coefficients for monochloronaphthalene and octachloronaphthalene which themselves had been calculated (rather than experimentally measured) using a method described by Hansch and Leo [88]. A less than satisfactory procedure but one that, in the absence of experimental data, at least provides values which may be used to make general predictions of the potential environmental behaviour of the compounds.

# 5. HUMAN HEALTH EFFECTS

## 5.1 INTRODUCTION

Concern over the toxicity potential of chloronaphthalenes arose as a result of the discovery of an association between often severe skin reactions in workers and occupational exposure to the compounds. The skin condition was referred to as a chloracne in 1899 by Herxheimer [89]. Although not exclusive to chloronaphthalene exposure, the disease was common among workers handling chlorinated naphthalenes in such operations as the sealing of electrical cables and components, the patching of sealed cables, the chromium plating industry, and the manufacturing of chloronaphthalenes. Chloracne could result both from skin contact and as a consequence of inhalation. It is only inhalation of chloronaphthalenes, as fumes arising from hot chloronaphthalene wax processing operations, which has been linked to liver disease. This toxicity was manifested as an acute yellow liver atrophy, and could lead to death. Other organ damage, especially that of the kidney, could also contribute to a fatal outcome.

Although the link between chloronaphthalenes and occupational disease is clear, dose-response predictions in humans are precluded by insufficient quantitative data. This need has led to a search for an animal model of toxicity. While it has been possible to match the types of toxicity effects recorded in humans using results from various laboratory and domestic animal species, no single test species appears to describe adequately the human response profile.

For animals in general, the literature shows that the tetra- to hexachloronaphthalenes are most toxic, and that there appears to be a dose-response relationship. Latent toxicity effects may be related to the accumulation of chloronaphthalenes in body stores. It also appears that the use-pattern of chloronaphthalenes in the manufacturing sector has changed to such a degree over the past decades that chloronaphthalene poisoning in workers has become highly uncommon or non-existent.

## 5.2 ACCUMULATION

The quantitative characteristics of chloronaphthalene uptake and distribution have been described in a small number of animal studies. Cleary et al. determined that chloronaphthalenes were readily absorbed from an olive oil solution when given in daily oral doses to rats [90]. Complete absorption was recorded for doses up to 15 mg per day; but no evidence of storage of the chlorinated naphthalenes was found in lung, liver, skin, or kidneys. The authors suggested that an effective metabolism limited the presence of benzene-soluble chlorinated compounds. As more recently reported, a single oral dose in rats of radiolabelled dichloronaphthalene (400 mg/kg) resulted in a rapid uptake of the compound [91]. It can be calculated from these data that one hour after ingestion approximately 17 percent of the dose was present in blood. By eight hours, radioactivity levels in the blood decreased to about two-thirds of that in the first hour post-dosing and declined greatly by 48 hours. Dichloronaphthalene-derived radioactivity was found also in a wide range of tissues and excretory products (Table 5-1). Radioactivity in tissues had decreased further by seven days post-dosing and was detectable only in adipose tissues and skin. Such selective retention has been attributed to the lipophilic nature of the chloronaphthalenes. Lipophilicity was also demonstrated when rats were given tetrachloronaphthalene in their daily diet at levels of 0.04 to 400 mg/kg food [92]. A plateau in adipose tissue and concentrations was achieved by five weeks. At equilibrium, adipose tissue levels can be calculated to be 97, 58 and 5.8 times greater than in blood on a unit weight basis, following administration of 400, 200 and 40 mg/kg tetrachloronaphthalene respectively. Accumulation from food followed the exponential relationship:

$$\text{Concentration in body tissue} = a.(\text{concentration in food})^{b}$$

where a and b are constants.

When both 1- and 2-chloronaphthalenes were administered separately to pigs at a single dose of 40 mg/kg body weight via the carotid artery, it was found subsequently that the chloronaphthalenes were widely distributed in

## TABLE 5-1 Tissue Distribution of Radioactivity in Rats Dosed with Carbon-14 Labelled Dichloronaphthalene*

| | A | | B | | C | |
|---|---|---|---|---|---|---|
| | DPM/mg | % | DPM/mg | % | DPM/mg | % |
| Blood** | | 6.1 | | 3.2 | | |
| Adipose | 8.1 | 0.1 | 11.7 | 0.15 | 3.26 | 0.04 |
| Lung | 14.1 | 0.04 | 14.3 | 0.03 | - | - |
| Liver | 21.3 | 0.7 | 34.3 | 0.07 | - | - |
| Bladder | 30.6 | 0.01 | 42.4 | 0.01 | - | - |
| Kidney | 39.6 | 0.18 | 46.5 | 0.15 | - | - |
| Intestine | 87.0 | 0.45 | 251.0 | 3.6 | - | - |
| Skin | 4.7 | 0.07 | 5.7 | 0.08 | 0.73 | 0.01 |
| GI-content | 1124.0 | 18.3 | 1963.0 | 17.9 | 7.6 | 0.04 |
| Fecal excretion | | 18.9 | | 30.8 | | 42.0 |
| Urine | | 26.4 | | 32.6 | | 35.2 |

(A) after 24 hours, (B) after 48 hours, and (C) after seven days of the dose being given.

Note: The animals were given a single oral dose of radiolabelled dichloronaphthalene. The values presented in the table are averages obtained from four or more animals and are expressed in DPM/mg of dried tissue and as a percentage of the total dose given. The standard deviations were within 40 percent of the mean values presented. (DPM = disintigrations per minute, and are a measure of the radioactivity residing in the tissue sample.)

* adapted from Chu _et al._ [91]

** estimated on the basis of data presented by Chu _et al._ [91] for blood radioactivity and using a rat weight of 300 g.

body tissues, both as the parent compound and the metabolized form [93]. Six hours after the injection, the two parent compounds were each found in brain, kidney, liver, lung, skeletal muscle, heart and fat, with highest concentrations in the brain and kidney. Concentrations in fat at six hours were the lowest, which is perhaps not surprising considering the limited circulatory perfusion of this tissue and the fact that, in this study, only one dose of the monochloronaphthalenes was given and this was measured after six hours.

A recent experiment examined the absorption of chloronaphthalenes into rat mitochondria [94]. Twenty-four hours following I.P. injection of the chloronaphthalenes at a dose of 7 g/kg body weight, liver mitochondria showed a selective uptake of the compounds. Chloronaphthalenes of lower chlorination were taken up to a greater degree than the more highly chlorinated compounds.

Although there are obvious limitations to drawing parallels between non-mammalian responses and those exhibited in mammalian tests, the lack of extensive data on chloronaphthalene absorption requires at least a limited perusal of the fairly detailed information gathered for some algal and invertebrate marine species. In four species of marine unicellular algae, accumulation of chlorinated naphthalene compounds (Halowax 1000, 1013 and 1014) appeared to be directly related to the chlorine content of the commercial products. The mono- and dichloronaphthalenes, however, were found to be the most toxic [95]. Shrimp (Palaemonetes pugis) exposed to three different Halowaxes (1000, 1013 and 1099) at 40 ppb (measured in water) showed a rapid accumulation of all three, reaching a plateau by three days [96]. Again, the more highly chlorinated naphthalenes accumulated to the greatest degree. For example, a concentration of 12 ppm in tissue (a bioconcentration factor of 300) was observed for Halowax 1099, a mixture of tri- and tetrachloronaphthalenes. When the effects of Halowax 1099 were tested in the horseshoe crab (Limulus polyphemus), it was found that the degree of bioconcentration by 96 days increased with levels in water (0, 22, 40 and 70 ppb nominal exposure, stated to have decreased greatly during exposure) to a maximum factor of 74 [97]. An additional point of interest revealed by this study was that the accumulation of the Halowax compounds was much less than from a similar dose of a polychlorinated biphenyl (Arochlor 1254).

Few absorption and accumulation data exist for human exposure studies. The suggestion is made that the contents of swollen sebaceous acini in chloracne episodes contain chlorinated naphthalenes. There appears to be a crystalline structure to the acinar contents which resembles that of the unchanged chlorinated naphthalene [98].

In general, it appears from the limited absorption information available that the various chloronaphthalenes are not accumulated to a great degree in tissues, with the possible exception of adipose tissue. The existence of an effective metabolic excretion mechanism is indicated.

## 5.3 METABOLISM AND EXCRETION

### 5.3.1 Metabolite Formation and Chloronapthalene Clearance

In 1939, Cleary *et al.* attributed their inability to detect significant benzene-extractable organic chlorine compounds in the tissues of rats which had been exposed to chloronaphthalenes to a metabolic dehalogenation [90]. No "organic chlorine" was found in the urine, although total urinary chlorine did increase and was sufficient to account for 60 per cent of the chloronaphthalenes ingested. A renal clearance mechanism can be suggested. Furthermore, the authors found that an oral dose (1 g) of mixed chloronaphthalenes in a dog resulted in a fourfold rise in urinary ethereal sulphate, indicating that excretion of chloronaphthalenes may be occurring by the formation of an organic sulphate compound.

A comprehensive study of urinary chloronaphthalene metabolites was carried out in rabbits, using a wide range of chlorinated naphthalenes [99]. The fate of the test compounds (administered in 1 g doses) was assessed in total 24-hour urine samples, taken before and after dosing. Table 5-2 indicates that rabbits can metabolize chloronaphthalenes, particularly the mono- and dichloronaphthalenes. Tetrachloronaphthalenes are metabolized to a lesser degree, while the more highly chlorinated naphthalenes did not show as urinary metabolites. The major excretory product in this study was glucosiduronic acid. Ethereal sulphate and mercapturic acid accounted for additional but smaller fractions of the excreted chloronaphthalene load. The suggestion was made that the diverse excretory potential for chloronaphthalenes correlates with the lower toxicity of the mono- and dichloronaphthalenes in mammals.

It was well demonstrated in rats that a single oral dose of 400 mg/kg body weight of carbon-14 labelled 1,2-dichloronaphthalene was eliminated primarily by way of urine and feces [91] (Table 5-1). Sixty-four percent of the dose was removed within two days by these two excretory modes, each about equally effective in the depuration process. The fecal route of loss was due to biliary action, although about one-third of the excretory products in bile were reabsorbed in the gut. Analysis of the feces of these radiolabelled 1,2-dichloronaphthalene exposed rats showed that the radioactivity was due to unchanged dichloronaphthalene. This suggests that the liver and gall bladder in the rat do not carry out metabolic conversions of chlorinated naphthalene in their excretion functions. Conversely, the metabolite associated with urine was neither dichloronaphthalene nor free chloronaphthol, but was the glucuronide of a dihydrodiol of dichloronaphthalene. A more detailed characterization of the urinary metabolites of dichloronaphthalene is presented by Chu et al. [100,101]. Rabbits and, in particular, rats were treated with a single oral dose (400 mg/kg body weight) of a dichloronaphthalene. The authors then isolated and identified urinary and fecal metabolites (Figure 5-1). Hydroxylation and/or hydroxylation-dechlorination were found to be common metabolic pathways. The

### TABLE 5-2 Effect of Ingestion of Naphthalene and Chlorinated Naphthalenes on Excretion of Urinary Metabolites by Rabbits [99]

| Compound Fed | Ethereal Sulphate | | Mercapturic Acid | | Glucuronic Acid | | Free Phenolic Compounds | | Total Excretion of Compound Fed | |
|---|---|---|---|---|---|---|---|---|---|---|
| Compound Fed | Sulphur mg* | Excretion of Compound Fed mg | Sulphur mg* | Excretion of Compound Fed mg | Total mg* | Excretion of Compound Fed mg | Total mg* | Excretion of Compound Fed mg | mg | % |
| **Naphthalene** | | | | | | | | | | |
| Control | 27 | | | 132 | | 632 | | 289 | | |
| Experimental | 43 | 64 | | 180 | 192 | 1224 | 390 | 306 | 23 669 | 67 |
| **1-Chloronaphthalene** | | | | | | | | | | |
| Control | 23 | | | 103 | | 661 | | 300 | | |
| Experimental | 44 | 101 | | 129 | 131 | 1301 | 537 | 312 | 20 789 | 79 |
| **Dichloronaphthalene** | | | | | | | | | | |
| Control | 26 | | | 109 | | 925 | | 284 | | |
| Experimental | 37 | 55 | | 141 | 177 | 1604 | 686 | 251 | 918 | 92 |
| **Tetrachloronaphthalene** | | | | | | | | | | |
| Control | 22 | | | 121 | | 455 | | 281 | | |
| Experimental | 27 | 40 | | 125 | 32 | 731 | 379 | 257 | 451 | 45 |
| **Pentachloronaphthalene** | | | | | | | | | | |
| Control | 29 | | | 109 | | 739 | | 351 | | |
| Experimental | 34 | | | 104 | | 759 | | 304 | | |
| **Heptachloronaphthalene** | | | | | | | | | | |
| Control | 43 | | | 100 | | 680 | | 381 | | |
| Experimental | 30 | | | 91 | | 698 | | 350 | | |
| **Octachloronaphthalene** | | | | | | | | | | |
| Control | 24 | | | 96 | | 881 | | 279 | | |
| Experimental | 31 | | 93 | | 670 | | 275 | | | |

* The values represent the total 4 day excretion, showing the average of results obtained from three different animals.

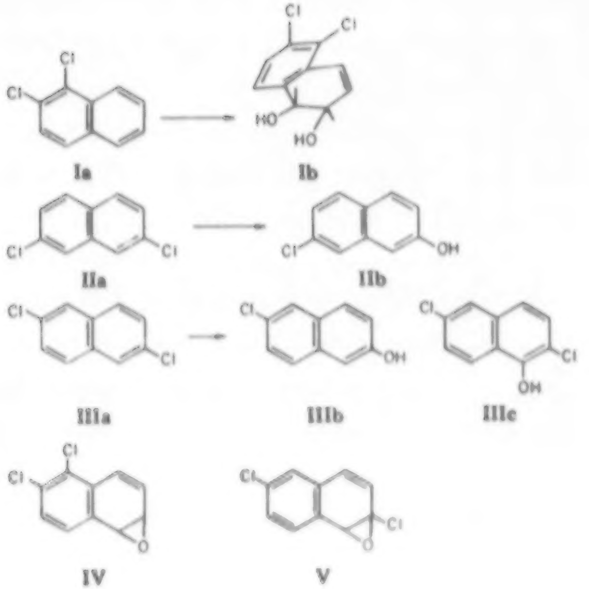


FIGURE 5-1 Metabolites of Three Dichloronaphthalenes Showing Excretory Products (Ib, IIb, IIIb and IIIc) and Arene Oxide Intermediates (IV and V) [101]

1,2-dichloronaphthalene was transformed to the glucuronide conjugate of 5,6-dichoro-1,2-dihydroxy-1,2-dihydronaphthalene (metabolite Ib). The 2,7-dichloronaphthalene was metabolized to free and conjugated 7-chloro-2-naphthol (metabolite IIb). The 2,6-dichloronaphthalene was metabolized to free and conjugated 6-chloro-2-naphthol (metabolite IIIb) and 2,6-dichloronaphthol (metabolite IIIc). Two arene oxides (IV and V) are suggested as intermediates in the formation of the dihydrodiol (Ib) and in the formation of 2,6-dichloronaphthol (IIIc) respectively.

An approach, which was similar to that in the determination of chloronaphthalene metabolites in rats, was used in studies on pigs by Ruzo and colleagues [93,102,103]. When pigs were given 1- or 2-chloronaphthalene at doses of 40 mg/kg body weight, administered via the carotid artery, metabolic conversion of the parent compounds commenced within three hours. The metabolites 4-chloro-1-naphthol and 3-chloro-2-naphthol were identified in blood, kidney and liver at low concentrations, and at high concentrations (up to 900 μg/g) in urine and bile [93,103]. Additional investigations into the conversion of chloronaphthalenes to urinary and bile metabolites yielded the results shown in Table 5-3. The major chloronaphthalene metabolites were phenolic products, although no metabolites were identified for hexachloronaphthalene. In contrast to findings by Chu et al. in the rat [101], no dechlorination was observed with any of the substrates investigated in this study using pigs. An arene oxide intermediate is also hypothesized in the metabolism of 1-chloro-4-[$^2$H]naphthalene and 1,4-dichloronaphthalene (Figure 5-2).

A number of investigations have shown that the metabolism of chloronaphthalenes also occurs in non-mammalian species. Studies in the leopard frog (Rana pipiens) showed that the administration of 1-chloronaphthalene (20-40 mg/frog, injected I.P. in peanut oil solution) led to the formation of one major phenolic metabolite, the 4-chloro-1-naphthol [104]. This metabolite was also found in pigs [93]. In frogs, injection of 1,4-dichloronaphthalene led to the metabolic formation of 2,4-dichloro-1-naphthol. Its formation also requires an arene oxide intermediate [104,105].

### TABLE 5-3 Halonaphthalene Metabolites Determined in Urine and Bile of the Pig*

| Substrate | Metabolite |
|---|---|
| 1-Chloro-4[$^{2}$H]naphthalene | 4-Chloronaphthol |
| 1,2-Dichloronaphthalene | 3,4-Dichloronaphthanol |
| 1,4-Dichloronaphthalene | 2,4-Dichloronaphthanol |
| 1,4-Dibromonaphthalene | 2,4-Dibromonaphthol<br>5,8-Dibromonaphthol |
| 1,2,3,4-Tetrachloronaphthalene | 5,6,7,8-Tetrachloronaphthol<br>5,6,7,8-Tetrachloro-2-naphthol |
| 1,2,3,4,5,6-Hexachloronaphthalene | none |

* excerpted from Ruzo *et al.* [102]

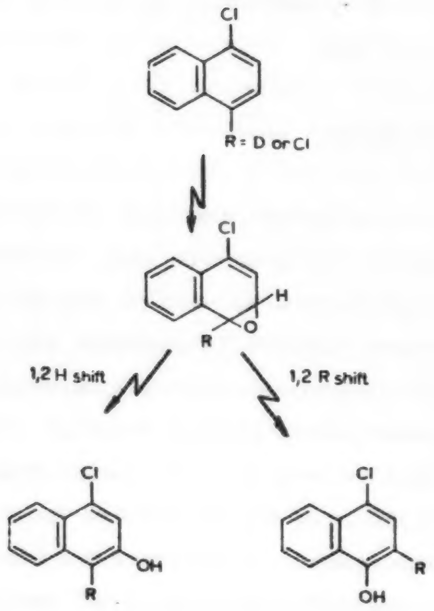


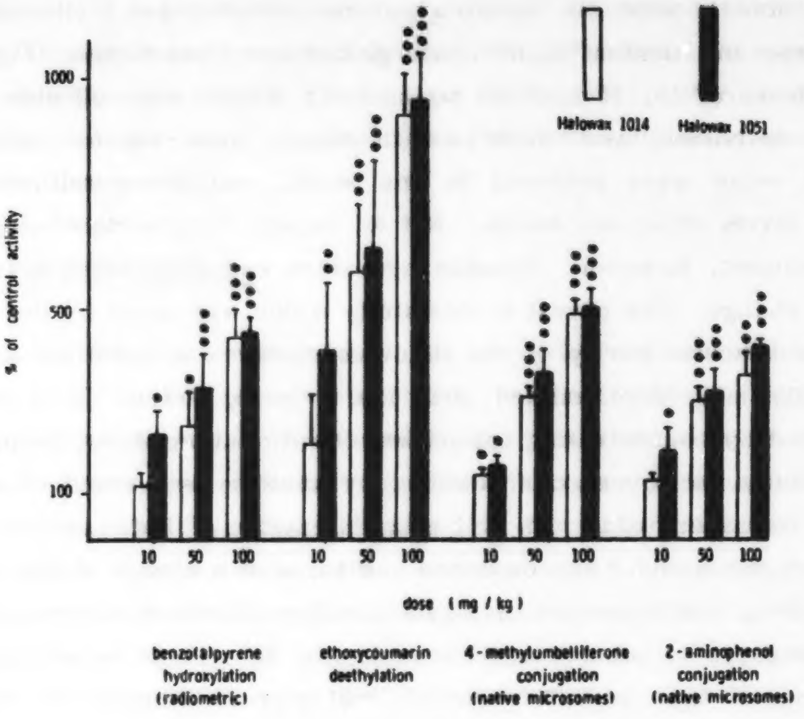
**FIGURE 5-2** Scheme for the Metabolism of 1-chloro-4-[$^{2}$H]naphthalene and 1,4-dichloronaphthalene in the Pig [102]

The ability to metabolize chlorinated naphthalenes is not even restricted to vertebrates. A rapid clearance of accumulated chloronaphthalenes in the horseshoe crab after exposure to Halowax 1000, 1013 and 1099 suggests an effective clearance mechanism (Green and Neff, 1977). Marine algae, as well, are postulated as possessing the ability to metabolize mono- and dichloronaphthalenes [95].

### 5.3.2 Enzymatic Mechanisms

Recent investigations using rats have identified chloronaphthalenes to be inducers of hepatic drug-metabolizing enzymes. Female rats given 1,2,3,4-tetrachloronaphthalene showed a significant increase in p-nitroanisole demethylase, and slight but consistent increases in the activity of all other mixed-function oxygenases examined (cytochrome P-450, cytochrome $b_5$, aminopyrine demethylase) [106]. Another study using rats reported only a minimal or selective response of hepatic drug-metabolizing enzymes to chloronaphthalenes [107]. Of the chloronaphthalenes tested (1-chloronaphthalene, 2-chloronaphthalene, 1,2-dichloronaphthalene, 1,4-dichloronaphthalene, and 1,2,3,4-tetrachloronaphthalene) and assessed for their ability to modify p-nitroanisole demethylase activity and EPN (phenylphosphonothioic acid O-ethyl-O-p-nitrophenyl ester) detoxication, only 1,2-dichloronaphthalene was reported to be effective. The activity of p-nitroanisole demethylase was stimulated at oral doses of 1000 ppm. Detoxification of EPN was not stimulated until a dose level of 5000 ppm was fed. When a series of Halowaxes was fed at 3000 ppm, enzyme activities increased with the degree of chlorination, but declined again using the most highly chlorinated chloronaphthalenes.

A detailed assessment of the enzyme inducing potential of a series of Halowaxes (1031, 1000, 1001, 1099, 1013, 1014, 1051), increasing in chlorine content from 22 to 70 per cent, was carried out in rats by Ahotupa and Aitio [108]. This comprehensive study identified that chlorinated naphthalenes with a high chlorine content, particularly Halowax 1014 and 1051, were potent inducers of enzymes catalyzing drug hydroxylation or glucuronidation in rat liver, such as benzo(a)pyrene hydroxylase, ethoxycourmarin deethylase and uridine diphosphate glucuronosyltransferase (Figure 5-3). Single doses of 10, 50 and 100 mg/kg body weight were all able to induce enzyme activities, and there was a direct dose-response relationship. Maximal rates were achieved in one week, and were maintained above control levels after one month. Not all hepatic drug-metabolizing enzymes were induced, however. Epoxide hydratase and glutathione S-transferase did not change. One caveat to this study which was noted by the authors is that the absolute purity of the Halowax mixtures was not known and the possibility may have existed that the inducing action could have been augmented by contaminating impurities. Confirmation of the findings of the above study, however, was obtained by another assessment of microsomal enzyme induction using rats and a similar series of Halowaxes [109]. The rats were injected I.P. on days one and three at a dosage of 150 μmol/kg or 600 μmol/kg, and examined on day six. The effects of chloronaphthalenes were compared to other enzyme inducers in an attempt to classify chloronaphthalenes into phenobarbitone-, methylcholanthrene- or mixed-type inducers. At the high dose level, all the Halowaxes enhanced microsomal benzo(a)pyrene hydroxylase activity, cytochrome P-450 content, and dimethylaminoantipyrine N-demethylase activity. The Halowaxes 1000, 1001 and 1099 were identified as belonging to the phenobarbitone-type of inducers, whereas Halowaxes 1013, 1014 and 1051 were mixed-type inducers. The significance of these differences awaits clarification. A further problem in interpretation is that the more highly chlorinated naphthalenes, which are most toxic, have the highest capability of causing enzyme induction, but no derived metabolites have yet been identified from this activity.



**NOTE:** Enzyme activities were measured 7 days after a single I.P. dose. The number of animals was 4. The significance is expressed as follows: * = $2P < 0.05$, ** = $2P < 0.01$, and *** = $2P < 0.001$ by Student's t-test.

**FIGURE 5-3** Effect of Various Doses of Highly Chlorinated Naphthalenes on the Activities of Enzymes Catalyzing Drug Hydroxylation or Glucuronidation in Rat Liver [108]

## 5.4 TOXICITY EFFECTS

### 5.4.1 Lethality

5.4.1.1 Human studies: Exposure to chloronaphthalenes has been demonstrated to be fatal to humans only when inhaled as fumes generated by manufacturing processes. The earliest reports are for three cases, reported by Flinn and Jarvik [110] and Drinker *et al.* [111]. The workmen had been exposed to tetra-, penta-, and/or hexachloronaphthalenes, and additionally, in one case, to chlorinated diphenyl. In all cases, death occurred after an acute illness characterized by jaundice, and autopsy revealed acute yellow atrophy of the liver. Other cases have subsequently been reported. Five workers using chloronaphthalenes in capacitor and wire or small parts coating processes became ill several months after exposure. The illnesses became severe and deaths due to acute liver failure occurred several months later [112-114]. Strauss details the case histories and post-mortem reports of an additional six workers who died showing acute yellow atrophy of the liver [115]. They had also been exposed to chloronaphthalene fumes during their employ.

Another study of the same era, in which the extensive use of chloronaphthalenes was predicated by the technological needs of the Second World War, assessed illness and fatality using an epidemiological approach [116]. Of 2500 men employed in the wire cable manufacturing industry (the wire was hot coated with chloronaphthalenes to render it heat resistant and water repellent), 450 were shown to be sensitive to the chlorinated naphthalenes. Seven of these died as a result of exposure. In all seven cases the illness developed in a matter of months. It was progressive and would not respond to treatment, even though the victims were removed from the exposure. Although the early reports suggested that young adults were more susceptible to serious consequences of exposure, an overview of all the reported fatalities suggests that there is no age distinction.

5.4.1.2 Animal studies: While it has been documented that exposure to chloronaphthalenes can be fatal in humans, it has not been possible to determine exposure concentrations at which these effects occurred. The various animal studies, using laboratory, domestic and wild species have shed some light on this problem. The following conclusions are based on the data summary presented in Table 5-4. In all of the laboratory and domestic species tested, only oral or I.P. dosing resulted in death. Inhalation or dermal exposures have not been found to be fatal [118]. Death generally takes several days, and may occur after a single dose. The primary factor responsible for the lethality is liver disease, marked as liver necrosis and yellow liver atrophy. No relationship can be expressed between the degree of chlorination and the time to death. An exception here may be the data for shrimp [96] which show a greater sensitivity to the more highly chlorinated naphthalenes, but any link to the human condition must be considered spurious.

It is of interest that the different species show their own unique sensitivities. Rabbits are more sensitive than rats, and both swine and sheep are much less sensitive than cattle. Cattle appear to be particularly easily affected by chloronaphthalenes, a condition which is expressed in the ramifications of bovine hyperkeratosis (section 5.4.4). Since test results appear to differ greatly among animal species, it is valid to assume that the responses of any individual species, including the laboratory rat, will not correspond to all the physiological effects of a toxicant in humans. It may be more practical to assess fully the hazards of such a contaminant as chloronaphthalene by examining many different species, thus presenting a wide spectrum of possible response types and intensities.

### 5.4.2 Clinical Symptoms of Systemic Poisoning

5.4.2.1 Human studies: Although most studies of chloronaphthalene toxicity in humans have concentrated their descriptions on more specific symptoms such as chloracne or hepatotoxicity, the various case histories in

**TABLE 5-4 Lethality Data for Polychloronaphthalene Exposure, from Studies on Animals**

| Species | Chloronaphthalene | Exposure Route | Dose Level (mg/kg) body weight* | Exposure Time (days) | Remarks | Source |
|---|---|---|---|---|---|---|
| rat | 1-mono | oral | 1,540 single | - | $LD_{50}$ | [117] |
| | 2-mono | oral | 2,080 single | - | $LD_{50}$ | |
| | penta/hexa | oral | 300/day | 33 | liver disease | [118] |
| | penta/hexa | oral | 100/day | 55 | liver disease | |
| | hexa | oral | 200 | 84 | | |
| rabbit | tetra/penta | I.P. | 15/day | 12-15 | liver disease | [110] |
| | penta/hexa | I.P. | 15/day | 12-26 | liver disease | |
| | octa | oral | 1000 single | - | death in 7 days | [118] |
| guinea pig | penta | oral | 2.5 | 48 | liver disease | " |
| cattle | hexa | oral | 9 single | - | 1.0 g per calf, death in 14 days | [119] |
| swine | hexa | oral | 176-220/day for 8-9 days | - | death in 33 to 40 days | [120,121] |
| sheep | penta/hexa | oral | 117/day | 106 | liver, heart and renal disease | [122] |
| | | | 301/day | 27 | | |
| | | | 563/day | 20 | | |
| turkey | penta/hexa | oral | 5 mg/kg feed | 33 | 5% mortality | [123] |
| | | | 100 mg/kg feed | | 100% mortality | |
| chicken | penta/hexa | oral | 20 mg/kg feed | 14 | 5% mortality | [124] |
| | | | 2,500 mg/kg feed | | 100% mortality | |
| frog | 1-mono | I.P. | 900 | - | $LD_{50}$ | [104] |
| shrimp | mono/di | in water | 325/440 µg/L | 4 | $LC_{50}$ | [96] |
| | tri/tetra | in water | 69/90 µg/L | 4 | $LC_{50}$ | |
| | tetra/penta | in water | 74 µg/L | 4 | $LC_{50}$ | |
| horseshoe crab | tri/tetra | in water | 80 µg/L | 27 | $LT_{50}$ | [97] |

* except as otherwise noted

the literature also report clinical symptoms attributable to a more general systemic poisoning. Table 5-5 summarizes the findings variously reported in the literature. The majority of the exposures were to chloronaphthalene fumes, generated in some heating operation associated with the specific manufacturing process. It is generally not possible to exclude completely dermal exposure and absorption since direct contact with a chloronaphthalene-coated product would have been difficult to avoid. Also, exposure by inhalation of dust, perhaps generated in some fabrication of chloronaphthalene products, would have involved dermal exposure as well.

The wide range of symptoms, summarized in Table 5-5, are presented in a general order of appearance, and are a consequence of continued exposure, or else are manifested in the progression of the disease. To the limited degree that an epidemiological assessment is possible, it appears that the majority of patients showed the less systemically severe symptoms. An examination of a situation in which 92 workers were exposed to a mixture of tetra- and pentachloronaphthalenes during the manufacture of chloronaphthalene-insulated electrical coils [128], revealed that a majority of workers showed skin lesions. Of 59 examined, 56 also showed clinical symptoms as follows: pruritis (itching), 39; eye irritation, 18; headache, 14; fatigue, 13; vertigo, 6; nausea, 3; weight loss, 3(or 1?); anorexia, 3; rhinitis, 1; and abdominal cramps, 1. In all instances, there was a latent period of a few to many months, after which time the more severe symptoms often continued to be expressed even if the patient were removed from the contaminant and hospitalized. This could be attributed, at least in part, to an only slow excretion of accumulated chloronaphthalenes. Although the earlier literature attributes some special sensitivity to young adults and women, a more complete overview of the data shows this not to be the case. A clear definition of sensitivities is confounded, however, by a lack of knowledge of exposure concentrations and exact chloronaphthalene composition.

The types of chloronaphthalenes causing these symptoms were the more highly chlorinated compounds. The point is made [128], that a test use of

### TABLE 5-5 Clinical Symptoms Associated with Occupational Exposure to Chloronaphthalenes

| Symptom* | References<br>[112] | [125] | [126] | [113, 114] | [127] | [115] | [116] | [98] | [128] |
|---|---|---|---|---|---|---|---|---|---|
| Itching | | I | | | D | I | | | I |
| Eye irritation | I | | | | D | | | | I |
| Weakness, lassitude | I | I | | | D | | I | I | I |
| Revulsion to smell of CN | | | | | | | I | | |
| Depression | | I | | | | | | | I |
| Headache | | | | | D | | | | I |
| Jaundice | I | I | I | I | | I | I | | |
| Impotence | | | | | D | | | | |
| Anorexia | I | I | I | I | D | I | I | I | I |
| Disturbance in taste | | | | | D | | | | |
| Nausea, dizziness | I | I | I | | D | | I | I | I |
| Dyspnea | I | | | | | I | I | | |
| Increased skin pigmentation | I | | | | | | I | | |
| Alopecia | | | | | D | | I | | |
| Puffiness of extremities | I | | I | I | | | | | |
| Abnormal liver | | | | | | I | I | | |
| Abdominal swelling and pain | I | | I | | | I | I | | I |
| Dark urine | | | | I | | I | I | | |
| Grey-yellow stools | | | | I | | I | I | | |
| Gastrointestinal distress, vomiting | I | | | I | | I | I | I | |
| Uncontrolled muscle movement | I | | | I | | | I | | |
| Coma and death | I | | | I | | I | I | | |

* symptoms are listed in the approximate order of their appearance

I exposure by inhalation
D dermal exposure

mono- and dichloronaphthalenes at a plant in a pilot study showed no deleterious effects. Later in production, however, the firm obtained and unwittingly used a product containing tetra- and pentachloronaphthalenes. This caused clinical symptoms as identified in Table 5-5.

Some of the clinical symptoms indicative of systemic poisoning can be linked to the more commonly described toxicity effects. For instance, pruritus and itching were secondary to the extensive manifestation of skin rashes, or to chloracne. Renal disease was implicated in the expressions of edema, while hepatotoxicity was suggested by jaundice, changes in liver size and dullness on palpation, a dark bilirubin-containing urine, and light coloured stools. A neurological effect of the icteric toxemia was an uncontrolled or even convulsive muscle movement which could be followed by a terminal coma. While the toxemia appears to come late in the clinical picture and thus may have contributed to renal failure, a renal involvement has also been suggested as an early effect. In one non-fatal case, the outstanding physical symptom was edema, which developed even before the icteroid scleral tinge [126]. The edema in this case was considered to be the result of a hypoproteinemia due to hepatic insufficiency.

A final point to be made is that systemic effects may develop from either inhalation or contact exposure. If from inhalation, they may precede the appearance of any skin lesions.

5.4.2.2 Animal studies: A number of the subjective clinical symptoms described in chloronaphthalene-poisoned humans have also been noted in animals. (The appearance of edema as a symptom is an example.) In cattle, for instance, the chloronaphthalene-induced X-disease which is characterized primarily by hyperkeratinization of the skin, commences with excessive lacrimation, diarrhea, polyuria, profuse salivation and serous nasal discharge. Later symptoms include a chronic cough, anorexia, weight loss, and red macular lesions in the buccal mucosa, as well as the skin changes. Terminal symptoms of X-disease were marked by a maintained urinating stance in cows, dehydration, weakness, and death [119,129-136].

Aside from the lethality of chloronaphthalenes in sheep as reported previously (Section 5.4.1.2), the onset of toxic signs was manifested in these animals by an excess serous nasal discharge, weakness, anorexia, weight loss, icterus, dyspnea and abdominal edema [122]. The sheep had been fed Halowax 1014 in their diet and showed symptoms at all doses tested (i.e., 117 to 563 mg Halowax/kg of body weight). Interestingly, the most obvious and prolonged symptoms of toxicity occurred at the low doses; a finding which still bears explanation.

When pigs (73 to 82 kg) were given daily oral doses (110 mg/kg of body weight) of hexachloronaphthalene, or were coated with the compound, they showed few overt signs of toxicity for several weeks [120]. Depression, diarrhea and anorexia were observed two to three days before the pigs became moribund. When young pigs, eight weeks of age and weighing 16 to 25 kg, were used, however, an exposure for eight to nine days to 22 mg/kg of hexachloronaphthalene resulted in signs of depression, anorexia and ataxia [121]. Retarded weight gain or weight loss was also common.

A pronounced edema, marked by hydropericardium and ascites (abdominal distension resulting from accumulation of serous fluid), was induced in chicks by feeding them penta- and hexachloronaphthalene in their diet [124].

While cattle appeared to be quite sensitive to chloronaphthalene poisoning, laboratory species such as the rat were much less so. Even massive inhalation exposures up to 10 mg/m$^3$ of air of tri-, tetra-, penta- and/or hexachloronaphthalenes given for several months resulted in little external expression of systemic toxicity [111]. The same researchers found that daily dietary exposures of between 50 and 300 mg per rat of the more highly chlorinated naphthalenes caused a general sickening and death of the animals within about two months [137]. (The cut-off point for lethality from ingestion of penta- and hexachloronaphthalene mixtures has been found to be 15 mg/day per rat [90].) This relative refractoriness of laboratory rats to chloronaphthalene poisoning points out the limitations of using this standard species in chloronaphthalene toxicity testing. Clearly data from other species as available must be used to understand the profile of chloronaphthalene toxicity.

### 5.4.3 Chloracne

5.4.3.1 Occupational: It is the condition of chloracne which initially drew attention to the toxicity of chloronaphthalenes to humans. The term was coined initially in 1899 by Herxheimer [89], and has been variously referred to as Perna-disease (from perchloronaphthalene [138]), Halowax acne, and "cable rash" [139]. The dominant lesion occurs at the skin, although many other sites may also be affected, in particular the renal system and the liver. Chloracne not only is specific to chlorinated naphthalenes but may also result from contact with other chlorinated organic compounds.

Occupationally, the disease has been found in workers who were exposed when manufacturing capacitors and coating electrical wires in which chloronaphthalenes were used [112,140]. Shipyard cable strippers also have been exposed in cable laying and patching operations [127,141]. Workers in the chloronaphthalene manufacturing industry were described as affected by chloracne [125], as were workers in chromium plating operations [114]. Chloracne has been observed in workers of leather and tent factories when chloronaphthalenes were used in material sealing processes. One reported case not directly of occupational origin was that of a child who contracted chloracne several months after his father sealed his featherbedding with a chloronaphthalene-containing cobblers wax [142].

Most occupational chloracne can be attributed to exposure through fumes from heated chloronaphthalenes or, less frequently, prolonged contact with cold chloronaphthalenes. Ingestion of chloronaphthalenes has also been identified to lead to chloracne. In 1945, six people were poisoned from eating food fried in an oil found in the Berlin ruins [143,144]. It was suggested that the oil contained hexachloronaphthalene. No deaths resulted, but general systemic symptoms were followed by severe chloracne. No recent outbreaks of chloronaphthalene-induced chloracne have occurred, which is in accord with the fact that chloronaphthalenes are only rarely or even no longer in industrial use.

Based on an overview of the cited literature on chloronaphthalene-induced chloracne and a review by Grimmer [98], it is evident that the severity of the effect is dependent, to a degree, on the duration and intensity of exposure. It is also probable that the exposed population exhibits some degree of individual sensitivity. The lack of extensive and controlled epidemiology for the condition prevents any conclusion on predisposition. The disease is identified as linked to the more highly chlorinated naphthalenes.

The clinical picture of occupational chloracne is as follows. The initial skin lesion is characterized as a reactive follicular hyperkeratosis marked by primary comedo formation in the pilosebaceous apparati of the skin. Secondary signs may develop to create a polymorphic clinical picture which includes the subjective and general systemic symptoms described previously (Section 5.4.3), as well as an elaboration of internal lesions.

Chloracneform eruptions may occur in any region of the body which contains hair follicles, although exposed skin areas have been most commonly affected. This includes facial skin, the side of the head including ears and external ear canal, the neck region, and arms and legs, especially in flexor regions. The genital regions are also frequently affected, possibly by a passive transport of chloronaphthalenes. A passive transport is also implicated in spreading of the disease to family members who were not otherwise exposed [98,127,145].

The progression of the disease has been identified by Grimmer (1955) as occurring in two distinct stages. The first stage, following a latency period of two to eight weeks, is an acute phase which is characterized by a photosensitivity. Exposure to light leads to often severe inflammatory reactions of the skin. Long wavelength ultraviolet light is suggested to be specific. Grimmer [98] interprets the vesicular erythematous dermatitis, described by Mayers and Silverberg [140] as a "cable rash" manifestation, as the early photosensitive phase of chloracne. One may extend the light dependency theory to explain an observation occasionally made in occupational chloracne case histories -- that the incidence of the disease appears to be greater in the summer. The photosensitive first stage of chloracne gives way with loss of the light reaction to a second stage, identified by Grimmer as the chronic phase. This phase is characterized by the formation of comedones in the sebaceous glands of hair follicles. The comedone formation is associated with a reactive hyperkeratosis of the follicular apparatus. The involvement progresses to secondary inflammatory processes which may develop within weeks into a polymorphic clinical picture. Histologically, as well as clinically, chloracne is a specific disease and not the same as acne vulgaris.

Secondary reactions to comedo formation may be staphylococcal infections, folliculitis, and transformation of hair follicles and sebaceous glands into keratinous cyst-structures. This may lead to further inflammatory reactions, vacuolar degeneration and edema. The lipoid comedo of chloracne may act as a storage site of chloronaphthalenes. An examination of comedo extracts by polarized light microscopy has confirmed polychloronaphthalene crystal structure similar to the chloronaphthalenes to which the patient had been occupationally exposed [98].

In summary, the appearance of chloracne following exposure to chloronaphthalenes may occur after a latency period of short but variable duration. The modes of exposure might be by way of dermal contact with chloronaphthalene dust or sublimated fumes, internal through inhalation of dust or fumes, otherwise through ingestion and absorption, or a combination of any or all of these. From the point of view of dose-response relationships or safe doses, little can be said that is truly definitive. Drinker and colleagues suggested highest permissible levels for trichloronaphthalene at 10 mg/m$^3$, for tetra- and pentachloronaphthalene at 1 mg/m$^3$, and for penta- and hexachloronaphthalene at 0.5 mg/m$^3$ [111]. Although the levels themselves have little correlative human exposure data, they at least point out the relationship existing between toxicity and degree of chlorination.

5.4.3.2 Experimental studies: The search for an animal model for the experimental production of chloracne has been of limited success. Only the dog and the rabbit have shown a reaction similar to that in humans. Braun was able to induce a characterisitic non-inflammatory follicular hyperkeratosis after chronic application of chloronaphthalene ointment to the skin of the ear in these animals [146]. In a test of a full series of chloronaphthalenes, mono- to octachlorine substituted, only the penta- and hexachloronaphthalene mixture (Halowax 1014) was able to produce chloracne in the rabbit pinna [147]. Chloracne has also been induced in the rabbit ear canal [148,149]. Halowax 1014 and hexachloronaphthalene were each applied topically and caused stimulation of the epithelium of the outer root sheath and sebaceous gland ducts and a diminution of sebaceous gland tissue in the pilosebaceous apparatus. This was followed by comedo formation. An uncommon late sequel was pustule formation. Sebaceous gland loss occurred as a result of an inability of sebaceous gland cells to regenerate. Monochloronaphthalene compounds were found to be not effective.

The experimental findings in rabbits are mirrored in the experimental development of chloracne in human volunteers [146,147,149,150]. Long-term daily applications of chloronaphthalenes were consistently successful in producing skin lesions representative of those observed in occupational exposures. Both inflammatory and non-inflammatory lesions were produced, forming comedones, papules, pustules, and cystic masses. Almost every area of the human body was tested by these authors and chloracne could be induced in all of them. The transformation of the comedo into an abscess was interpreted as a primary chemical effect of the chloronaphthalene [147].

### 5.4.4. Systemic Effects: Hepatotoxicity

5.4.4.1 Occupational exposures: There is no doubt of the ability of chloronaphthalenes to cause extensive necrotic or resorptive damage to internal organs (Table 5-6). An acute icteric toxemia has frequently been identified as the ultimate factor causing death (Section 5.2). Many of the case histories describing chloracne do not identify a jaundice, suggesting that at least exogenous exposure to chloronaphthalenes may result in chloracne without a systemic effect. Hepatotoxicity has been associated with endogenous exposures, mainly through the inhalation of fumes from hot chloronaphthalene wax.

The disease is most often described as an acute yellow atrophy of the liver, a relatively rare disease. Flinn and Jarvik [110] (detailed in Drinker et al. [111], and in Greenburg et al. [112]) describe three fatalities following occupational exposure to tetra-, penta- or hexachloronaphthalene (chlorodiphenyl was also involved in one case). Their diagnosis was acute yellow hepatic atrophy. Hepatotoxicity was not necessarily fatal, and Drinker et al. [111] refer to four cases of non-fatal jaundice in chloronaphthalene exposed workers. Further clinical data are given for an additional three fatal cases by Greenburg et al. [112]. Strauss presented one new case and greatly detailed the case histories of six previously reported fatalities [115]. Careful investigation determined that the sole poisoning agent was a commercial chloronaphthalene, specifically a mixture of predominantly tri- and tetrachloronaphthalenes. Clinical liver function tests verified impaired hepatic capacity, although both the gross and histopathological picture of the liver showed yellow areas or islands of actively regenerating liver tissue. The toxic chemical had, however, destroyed most of the liver cells, leaving intact their supporting stroma, blood vessels and bile ducts.

**TABLE 5-6 Occurrence of Systemic Pathology in Various Organs (from studies of occupational exposures)**

| | Reference | | | | | |
|---|---|---|---|---|---|---|
| Organ | [110] | [111] | [112] | [115] | [113] | [116] |
| Liver | x | x | x | x | x | x |
| Kidney | | | x | | | |
| Pancreas | | | x | x | x | |
| Spleen | | | | | | |
| Gut | | | x | x | | |
| Adrenals | | | x | | | |
| Lymph nodes | | | x | | | |
| Heart | | | x | x | x | |
| Lungs | | | x | x | x | |

The rapid progression of the acute hepatotoxicity has been well described by McLetchie and Robertson [113] in a case of a woman exposed to chloronaphthalene fumes. After feeling unwell for eight weeks, the woman was admitted to hospital, at which time the degree of icterus was not extensive, although bile was present in urine. This did not change for three days, then the patient became highly icteric and progressed to coma and death in two days. The finding on necropsy was a very small, soft, shapeless and collapsed liver under a wrinkled capsule, showing a few firmer small yellow areas. Histologically, the liver showed a varying picture of acute damage, fibrous proliferation, and regeneration.

The epidemiological study by Cotter [116] of U.S. Navy workers conclusively places the development of liver disease as a late symptom of chloronaphthalene poisoning. Jaundice was shown to occur after prolonged exposure in sensitive individuals and fatalities were always associated with liver damage. The liver histopathology in these instances was also variable, as described earlier, showing a complete absence of liver cells and collapse of the stroma in some areas and regeneration in others. Clinical examination of plasma chemical parameters, when carried out, consistently verified the hepatotoxicity [112,115,116].

5.4.4.2 Animal studies: There has been consistently greater success in demonstrating hepatotoxicity in animals than was the case for chloracne induction. Liver damage has resulted from chloronaphthalene exposure in both domestic and laboratory animals (Table 5-7).

The extensive syndrome of X-disease in cattle (bovine hyperkeratosis) includes central lobular degeneration of liver cells, with bile duct proliferation [119,130,132,136]. Experimental studies in pigs [120,121] and sheep [122] demonstrated histological changes of a degenerative character. The highly chlorinated naphthalenes, particularly penta- to heptachloronaphthalenes, were most damaging. Vitamin A levels in plasma decreased, as was also demonstrated in bovine hyperkeratosis. It could be postulated that an

TABLE 5-7 Occurrence of Systemic Pathology in Liver and Other Organs (from studies in animal species)

| Species | Exposure Data* | Organs Affected** | | | | | | | | | | | References |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Liv. | Kid. | Pan. | Spl. | Ads. | Gut | Gall | Hrt. | Lung | Lym. | Rep. | |
| cattle | penta-CN; orally 2 to 8 g/day to termination | x | x | x | | | | | | | | | [130] |
| cattle | di- to octa-CN (pure cpds.); orally 5.5 to 50 mg total/kg body weight for 1 to 30 days | x | x | | | | x | x | | | | | [119] |
| cattle | penta- and hexa-CN; orally 0 and 50 to 200 mg daily for approx. 7 weeks | | | x | | | | x | | | | x | [151] |
| cattle | hyperkeratosis review; highly chlorinated CN's implicated | x | | x | | | x | | | | | x | [131] |
| cattle | active agent not identified, suggested to be CN by authors | | | | | | x | | | | x | | [135] |
| cattle | penta-CN; incidental contamination from air | x | x | | | | | | | x | | | [136] |
| pig | hexa-CN; orally 0 to 198 mg total/kg body weight for 8 to 9 days: penta-CN topical several times | x | | | | | | | | | | x | [120] |
| pig | hexa-CN; orally 22 mg/kg body weight, daily 8 to 9 days | x | x | | | | x | | | | | x | [121] |
| sheep | Halowax 1014; orally in feed 1.1 to 31.25 kg/mg body weight per day to termination | x | x | | x | x | x | x | x | x | | x | [122] |
| chicken | Halowax 1014; orally 0 to 2500 mg/kg feed, daily to termination | x | | | | | | | | | | | [124] |
| turkey | Halowax 1014 and 1051; orally 0 to 100 mg/kg feed, daily to termination | x | | | | | | | | | | | [123] |
| rabbit | tri- to hexa-CN; S.C. injection, 30 mg daily to termination | x | | | | | | | | | | | [110] |
| rat | tri- to hexa-CN; inhalation, ave. 1.2 mg/m$^3$; daily to termination | x | | | | | | | | | | | [111] |
| rat | tri- to hexa-CN; inhalation, 0.57 to 10.97 mg/m$^3$; also in diet; daily to termination | x | | | | | | | | | | | [137] |

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* CN = chloronaphthalenes; Halowax 1014 is a mixture of penta- and hexa-CN; Halowax 1051 is mainly octa-CN.

** Liv. = Liver, Kid. = Kidney; Pan. = Pancreas; Spl. = Spleen; Ads. = Adrenals; Gall = Gall Bladder; Hrt. = Heart; Lym. = Lymph Nodes; Rep. = Reproductive Tract extensive liver damage and resorption so decreased the storage potential for vitamin A in that tissue that plasma levels declined. Vitamin A therapy was generally not effective.

In poultry as well, chloronaphthalenes produced liver damage, marked by an enlarged liver with evidence of fibrosis [123,124]. Vitamin A storage varied inversely with the degree of chloronaphthalene exposure. Halowax 1014 was most hepatotoxic.

Laboratory tests for hepatotoxicity by chloronaphthalenes showed that yellow atrophy of the liver could be produced in rabbits [110], and in rats [111,137], either by oral dosing or by injection. The pathology mirrors that found in occupational fatalities. Liver size was diminished, the liver parenchyma had disappeared in many areas in which the stroma was collapsed; yellow regenerative patches were seen in others. One of the few recent related discoveries has been that chloronaphthalenes cause a decrease in cellular respiration of rat hepatic mitochondria, in proportion to dose. This effect was found both *in vitro* [152] and *in vivo* [94]. The *in vivo* effect was demonstrated within one hour of chloro-naphthalene injection. It is tempting to speculate that it is this biochemical lesion which eventually leads to the resorption of liver parenchyma cells observed histologically in other studies.

### 5.4.5 Systemic Effects: Other Pathologies

While most attention has been directed to hepatotoxicity, necropsy findings have shown that many other organs may also be involved. A review of necropsy reports of occupational exposures (Table 5-6) identifies a common involvement of the pancreas, showing edema, degeneration of the cells of the acini and islets, and a fatty necrosis. In a few instances, kidney damage is reported, showing glomerular and tubular degeneration. The adrenals may undergo a parenchymatous degeneration. Lymph nodes may be swollen. Hypertrophy of the heart was identified. The lungs showed edema in several instances and the gut mucosa was affected, showing evidence of inflammation, hypertrophy and hemmorhage.

All of the domestic animal species (Table 5-7) showed a potential for kidney damage, marked by a glomerular edema and tubular degeneration. Cows exhibited a pancreatic edema, as well as fibrosis and a degeneration of acinar cells. Lymph nodes were swollen. The gut mucosa was often affected by inflammation and cystic dilation of digestive glands. Gall bladder distension and wall thickening were found. Abnormalities of the reproductive tract developed in cattle, pigs, and sheep, marked by swelling and squamous metaplasia of the epididymides, seminal vesicles, and vagina. In sheep, uterine congestion and hemorrhage were common. Also in sheep, hemorrhage and congestion occurred in the spleen, adrenals, heart and lungs. The patchy record for these various organ pathologies is probably partly due to differential responses among species, differences in treatments, and inconsistencies in the clinical investigative format.

### 5.4.6 Reproductive Abnormalities

The reproductive tract abnormalities just identified (Section 5.4.4.2) for cattle, pigs and sheep (i.e., squamous metaplasia of seminal vesicles, epididymides and vaginal wall, uterine congestion and hemorrhage, as well as testicular degeneration) may be linked to reports in the literature of decreased sperm production in bulls [151] and abortion in cows and ewes [122,135]. Milk production also was decreased in cattle suffering from bovine hyperkeratosis [119].

Chickens were assessed for egg production when exposed to Halowax 1014 [124]. The dose-response relationship was as follows: 2500 ppm, lethal to hen; 100 ppm to 28 weeks of age, prevented egg production; 20 ppm, poor hatchability; 4 ppm, no effect. The 20 ppm dose in the pullets was embryotoxic to 84 per cent of the eggs laid. It was not identified if the effect was in the laying hen, or was teratogenic. The only other available information suggesting that chloronaphthalenes have a teratogenic effect is a study in frogs [153]. Tadpoles of Rana agilis were exposed to concentrations of 0.1 and 0.05 ppm Halowax 1014 in water. The 0.1 ppm dose was fatal to 52 per cent of the larvae after 18 hours, while the rest of the treated tadpoles delayed their metamorphosis for three weeks. A lesion at the endocrine level was suggested by histological changes in the endocrine (thyroid?) glands.

Altogether, few controlled or epidemiological studies on reproductive effects are available. The information is inadequate for the elucidation of a mechanism of action.

## 5.5 SUMMARY

The concern over chloronaphthalene poisoning in humans resulted from the occurrence of skin disease (chloracne) and systemic effects in workers, attributable to contact with, and/or inhalation of, chloronaphthalenes in the course of various manufacturing processes. A chloracne or "cable rash" was a common result of prolonged skin contact with chlorinated naphthalenes, linked to some degree with poor hygienic habits. The skin disease was marked by the formation of comedones in the acini of pilosebaceous glands of the skin, progressing to inflammatory reactions and gland destruction.

Systemic responses have been shown to involve a wide range of tissues and organs and could be seriously debilitating with progressive renal and hepatic damage. Fatalities were correlated with inhalation of chloronaphthalene fumes, associated with extensive tissue and organ lesions, particularly a yellow liver atrophy marked clinically by icterus. Many case histories report extensive liver damage and death to be a latent response, occurring weeks to months after removal from the source of chloronaphthalene poisoning. This may be attributed to a continued release into circulation of chloronaphthalenes from storage in fatty tissues. Recovery from chloronaphthalene poisoning, whether the manifestations were chloracne or systemic effects, generally ranged from several months to over a year.

There has been no quantification of occupational exposure levels resulting in toxicity responses in humans. Toxicity studies in laboratory animals, and comparative assessments of exposures in domestic animal species, have tried to model toxicity responses in humans and to establish dose-response relationships. The laboratory rat was found to be relatively refractory to chloronaphthalene exposure, surviving dietary exposures of 15 mg/day per rat and inhalation levels of 10 $mg/m^3$ for several months without untoward signs of intoxication. Cattle show another extreme, being highly sensitive and exhibiting bovine hyperkeratosis (X-disease) at very low-level exposures, and death after a single exposure of 1.0 g in the calf. Altogether, the various species differ greatly both in sensitivity to chloronaphthalenes and in the expression of toxicity. The rabbit was determined to be the most suitable for demonstrating chloracne. No single species, however, was found to exhibit all of the responses recorded in humans.

Chloronaphthalenes can be absorbed through the skin, lungs and gut, and tend to deposit in lipidic sites. Accumulation occurs in pilosebaceous acini and adipose tissue, and to a lesser degree in brain, kidney and other body tissues. Excretion occurs through urine and bile, and predominantly by the urinary excretion of conjugated metabolites. Hepatic microsomal oxygenases have been shown to be inducible by chlorinated naphthalenes, but the relationship of these reactions to chloronaphthalene detoxification, or perhaps a potentiation of chloronaphthalene toxicity, has not yet been defined.

Although the animal data are disparate it is possible to say that, in combination with findings from occupational exposures, the mono- and dichloronaphthalenes are relatively non-toxic or of low toxicity. This also tends to be the case for octachloronaphthalene. It is the tetra-, penta- and hexachloronaphthalenes which contribute most to chloronaphthalene toxicity. A dose-response relationship is suggested, although it is not possible to quantify this for human exposures. In humans, the toxicity effects of chloronaphthalenes tend to be progressive, becoming generalized to encompass many organs and systems at high doses. No sex or age dependency to the manifestation of toxicity has been confirmed in the occupationally exposed population.

A conclusion which might be reached from a survey of the available clinical literature, the past use patterns of the compounds, and the very low concentrations encountered in the environment, is that chloronaphthalenes are not likely to present a toxicity problem to the Canadian population. A caveat, though, is in order -- there are no studies from which the effects, if any, of continuous long-term exposure to very low concentrations of the compounds can be predicted.

# 6. REGULATIONS AND GUIDELINES

Information regarding regulations, standards and guidelines governing the use of toxic substances is not often readily available in the literature. For this reason, the Monitoring and Criteria Division of the Department of National Health and Welfare approached, on our behalf, the International Register of Potentially Toxic Chemicals (IRPTC), in Geneva, requesting information on regulations pertaining to chloronaphthalenes in member countries. Response was disappointing, only two countries (Japan and the United States) replied. This lack of response, however, may indicate only that few countries have legislation specifically dealing with chloronaphthalenes.

The occupational health area, however, is somewhat better served. The American Conference of Governmental Industrial Hygienists publish occupational exposure guidelines, Threshold Limit Values (TLVs®), for toxic substances (including some chloronaphthalenes) in the workroom environment. A number of countries and some Canadian provinces adopt TLVs® in their occupational health legislation.

## 6.1 ACGIH THRESHOLD LIMIT VALUES

The current TLVs® for chloronaphthalenes [154] are shown in Table 6-1. The criteria on which these TLVs® are based are outlined in the Documentation of the Threshold Limit Values for Substances in Workroom Air [155]. Hexa- and octachloronaphthalene are designated as substances for which there is a potential contribution to the overall exposure by the cutaneous route, either by airborne forms of the substances or, more particularly, by direct contact with the substances.

TABLE 6-1 Threshold Limit Values (TLVs®) for Chloronaphthalenes [154]

| Chloronaphthalene | TLV®-TWA<br>mg/m³ | TLV®-STEL<br>mg/m³ |
|---|---|---|
| trichloronaphthalenes | 5 | 10 |
| tetrachloronaphthalenes | 2 | 4 |
| pentachloronaphthalenes | 0.5 | 2 |
| hexachloronaphthalenes* | 0.2 | 0.6 |
| octachloronaphthalenes* | 0.1 | 0.3 |

* Designated as substances for which there is a potential contribution to overall exposure by the cutaneous route.

TLV®-TWA Time weighted average concentration for a normal eight-hour workday or 40-hour workweek, to which nearly all workers may be repeatedly exposed, day after day, without adverse effect.

TLV®-STEL The maximal concentration to which workers can be exposed for a period up to 15 minutes continuously without suffering from 1) irritation, 2) chronic or irreversible tissue change, or 3) narcosis of sufficient degree to increase accident proneness, impair self-rescue, or materially reduce work efficiency, provided that no more than four exposures per day are permitted, with at least 60 minutes between exposure periods, and provided that the daily TLV®-TWA also is not exceeded.

## 6.2 NATIONAL JURISDICTIONS

### 6.2.1 Canada

Although chloronaphthalenes were scheduled as Candidate Chemicals* under the Environment Contaminants Act [156], the substances are not included on the latest (1982) List of Candidate Chemicals [157]. With the lapsing of the reporting requirement for chloronaphthalenes (outlined in Section 3.2) in 1981, only the general requirements of the Environmental Contaminants Act [158] apply, in particular:

> Where during a calendar year, a person manufactures a chemical compound in excess of five hundred kilograms and he manufactures or imports that compound in excess of that quantity for the first time, he shall, within three months of manufacturing or importing the said quantity, notify the Minister (of the Environment) of the name of the compound, of the quantity manufactured or imported during that year and of any information in his possession respecting any danger to human health or the environment posed by the compound. [23-24 ELIZ. II, c. 72, s. 4(6)].

### 6.2.2 United States

The information in this section was provided by the United States correspondent to the IRPTC [159].

6.2.2.1 Occupational Safety and Health Administration (OSHA): Current OSHA standards in terms of permissible exposure limits in the workplace are in effect for five classes of chloronaphthalenes, grouped according to the extent of chlorination. The exposure limits range from 5 mg/m$^3$ (8 hr. TWA) for trichloronaphthalenes to 0.1 mg/m$^3$ for octachloronaphthalene [29 CFR 1910.1000] and are, in fact, identical to the TLV®-TWAs presented in Table 6-1.

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* Candidate chemicals are substances which may pose potential environmental contamination problems, but for which the degree of concern is insufficient to warrant placement on the List of Priority Chemicals (compounds for which regulation or control strategies are contemplated or for which information concerning commercial-use patterns, biological effects and environmental behaviour is actively sought) [157].

6.2.2.2 Environmental Protection Agency (EPA): The EPA administers a number of Acts dealing with the protection of the U.S. environment. At the present time, chloronaphthalenes are mentioned specifically in four Acts: the Federal Water Pollution Control Act, the Clean Water Act, the Resource Conservation and Recovery Act, and the Toxic Substances Control Act.

Only one chloronaphthalene, 2-chloronaphthalene is listed as a toxic pollutant under the Federal Water Pollution Control Act [40 CFR 401.15]. However, no effluent guidelines specifically limit discharge of this chemical at present.

A Water Quality Criteria document [45] was published for chloronaphthalenes [pursuant to Section 304 (a) (1) of the Clean Water Act]. However, no criterion for human health could be derived because of lack of data on these substances [Federal Register, 45:79318 (1980)].

One chlorinated naphthalene, 2-chloronaphthalene, is identified as a hazardous toxic waste under Section 3001 of the Resource Conservation and Recovery Act [40 CFR 261.33(f)], if it is a discarded commercial chemical product or manufacturing intermediate, or contained in clean-up residue resulting from a spill of the chemical in the form of a commercial product. Wastes under Section 3001 are subject to a "cradle-to-grave" management system which includes generation, transportation, treatment, storage, or disposal. An exclusion from compliance, however, is available for those enterprises who generate less than 1000 kg/month -- a situation which certainly now exists for chloronaphthalenes.

Chemicals perceived to be potentially toxic are recommended for testing by the Interagency Testing Committee under section 4(e) of the Toxic Substances Control Act -- and, indeed, chloronaphthalenes were recommended for such testing in 1978 [Federal Register, 43:16684 (1978)]. However, because chloronaphthalenes are no longer produced in the United States and import quantities are small, EPA has now concluded that such testing would not be required [Federal Register, 46:54491 (1981)].

### 6.2.3 Japan [160,161]

Chloronaphthalenes which contain more than three chlorine atoms (i.e., tetra- to octachloronaphthalenes) were designated as Specified Chemicals under the Law Concerning the Examination and Regulation of Manufacture, etc., of Chemical Substances in 1979. Specified Chemicals are those substances which are determined by the Japanese government to be chronically toxic and to have a high bioaccumulation potential. Chloronaphthalenes, one of only three classes of chemicals to have received such designation (the other two are polychlorinated biphenyls and hexa-chlorobenzene), are restricted in their production and import. Furthermore, their production, import and use are approved only where they cannot be substituted and are indispensible, and all handling has to occur in totally closed systems.

Organochlorine compounds, in general, are substances which are regulated in Japan with regard to "ocean dumping" and "incineration on the sea" under the Waste Disposal and Public Cleansing Law and the Law Relating to the Prevention of Marine Pollution and Maritime Disaster, respectively. Chloronaphthalenes would, of course, be affected by these laws.

### 6.2.4 Other Countries

Sweden has an eight-hour TWA exposure limit of 0.2 mg/m$^3$ with a STEL of 0.6 mg/m$^3$ for combined chloronaphthalenes; i.e., the sum of the concentrations of the individual chloronaphthalenes cannot exceed 0.2 mg/m$^3$ TWA or 0.6 mg/m$^3$ STEL in workplace ambient air [23,162]. Occupational exposure limits for chloronaphthalenes in the U.S.S.R. and East Germany are 0.5 mg/m$^3$ and 1 mg/m$^3$, respectively [24].

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# APPENDIX

## COMPANIES AND ORGANIZATIONS CONTACTED

Canada Colour Ltd., Toronto, ONT.
Dominion Colour Ltd., Toronto, ONT.
Dow Chemical Canada Inc., Sarnia, ONT.
Fischer Scientific Laboratories Ltd., Toronto, ONT.
General Electric Company of Canada, Peterborough, ONT.
General Motors of Canada, Oshawa, ONT.
Harrison and Crossfield Ltd., Toronto, ONT.
Koppers Chemical Company Inc., Bridgetown, PA.
Motor Vehicle Manufacturers Association, Toronto, ONT.
Record Chemical Company, Montreal, PQ.
Society of Plastics Industries in Canada, Toronto, ONT.
Sprague Electric Co., Mississauga, ONT.
Westinghouse Canada, Renfrew, ONT.